Access DB# 46842

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SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: FONDA Examiner #: 71970 Date: 7-16-01
Art Unit: 1623 Phone Number 308-1620 Serial Number: 09/550857
Mail Box and Bldg/Room Location: CM1 Results Format Preferred (circle): PAPER DISK E-MAIL
8B09 8A05

If more than one search is submitted, please prioritize searches in order of need.

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc. if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): ~~See bib. assignee sheets attached.~~

Earliest Priority Filing Date: _____

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please search for a solid composition comprising a therapeutic agent and a carbohydrate binder. The composition must also comprise a non-crystallization agent. See claim 21 for binder examples, and claim 24 for non-crystallization agent examples. The rapeutic agent can be virtually anything - see claims 32-35. I also need a method of making the composition (just mix, shape, and cool per claim 40), and an injection device per claim 56 that can inject the composition.

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PTO-1590 (1-2000)

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L73 ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2001 ACS
AN 2001:380434 HCAPLUS
DN 134:371815
TI Stable **amorphous** amifostine composition, and preparation thereof
IN Stogniew, Martin; Zadei, Javad M.
PA Medimmune Oncology, Inc., USA
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K047-18
ICS A61K009-19; A61K031-66; C07F009-165
CC **63-6** (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001035999	A1	20010525	WO 2000-US31495	20001116

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-440650 A 19991116
AB The present invention relates to a sterile, stable dosage form suitable for reconstitution and **parenteral** administration to a patient, said dosage form comprising and **amorphous** aminoalkyl dihydrogen phosphorothioate, amifostine in particular. The invention further relates to a method of prepg. such a dosage form, which typically exhibits enhanced thermal stability as compared to existing vacuum dried **amorphous** amifostine. An aq. soln. contg. amifostine 100 mg/mL and nicotinamide 12.5 mg/mL was filtered and freeze-dried.
ST freeze dried **amorphous** amifostine stabilizer

IT Drug delivery systems
(freeze-dried; stable **amorphous** amifostine compns. contg. stabilizers and excipients for reconstitution)
IT Amides, biological studies
Amino acids, biological studies
Gelatins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stable **amorphous** amifostine compns. contg. stabilizers and excipients for reconstitution)
IT **50-70-4**, **Sorbitol**, biological studies **50-99-7**, Dextrose, biological studies 56-40-6, Glycine, biological studies 56-41-7, Alanine, biological studies **57-50-1**, **Sucrose**, biological studies 59-67-6, Nicotinic acid, biological studies 60-00-4, Ethylenediamine tetraacetic acid, biological studies 61-90-5, Leucine, biological studies 63-91-2, Phenylalanine, biological studies 67-43-6, Diethylenetriaminepentaacetic acid **69-65-8**, **Mannitol** 70-47-3, Asparagine, biological studies 72-18-4, Valine, biological studies 73-22-3, Tryptophan, biological studies 73-32-5, Isoleucine, biological studies 77-92-9, Citric acid, biological studies 87-69-4, Tartaric acid 87-89-8, Inositol 98-92-0, Nicotinamide 145-42-6, Sodium taurocholate 302-95-4, Sodium deoxycholate 7647-14-5, Sodium chloride, biological studies 9003-39-8, PVP 9004-32-4, Sodium CMC **9004-54-0**, **Dextran**, biological studies 20537-88-6, Amifostine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stable **amorphous** amifostine compns. contg. stabilizers and excipients for reconstitution)
RE.CNT 7
RE
(1) Bioscience Inc; WO 9403179 A1 1994 HCAPLUS
(2) Bioscience Inc; WO 9834622 A1 1998 HCAPLUS
(3) Bioscience Inc; WO 0029025 A1 2000 HCAPLUS
(4) Jahansouz, H; Pharmaceutical Research, abstract No PDD 7336 1990, V7(9 Suppl), PS-195
(5) Kennedy; US 5424471 A 1995 HCAPLUS
(6) Kennedy; US 5591731 A 1997 HCAPLUS
(7) Zadeii, J; Pharmaceutical Research, abstract No PDD 7184 1991, V8(10 Suppl), PS172

L73 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:814284 HCAPLUS
DN 133:366419
TI Lipid particles on the basis of mixtures of liquid and solid lipids and method for producing same for drug delivery
IN Muller, Rainer Helmut; Jenning, Volkhard; Mader, Karsten; Lippacher, Andreas
PA Pharmasol G.m.b.H., Germany
SO PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DT Patent
LA German
IC ICM A61K009-16
ICS A61K009-50
CC **63-6** (Pharmaceuticals)
Section cross-reference(s): 2, 62
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000067728	A2	20001116	WO 2000-EP4112	20000508

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,

DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
DE 19938371 A1 20010222 DE 1999-19938371 19990809
DE 19945203 A1 20001221 DE 1999-19945203 19990921
PRAI DE 1999-19921034 A 19990507
DE 1999-19938371 A 19990809
DE 1999-19945203 A 19990921
DE 2000-10016357 A 20000331

AB The invention relates to lipid particles which do or do not carry active agents and comprise a mixed matrix consisting of solid and liq. lipid (so-called solid/liq. particles). The inventive particles are provided with a disordered structure (semicryst., mostly non-cryst. to **amorphous**) in the semisolid to solid condition. The invention also relates to a method for producing said dispersions and esp. a method for producing highly concd. lipid particle dispersions with a lipid content of 30 % to 95 % or a solids content of 30 % to 95 % (lipid and stabilizer). Said dispersions are integral particles unlike the biamphiphilic creams and/or the highly concd. particle dispersions result in free-flowing particle dispersions when dild. with the outer phase.

ST lipid particle prodn drug delivery

IT Diglycerides
Glycerides, biological studies
Monoglycerides
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(C16-18 monoglycerides and diglycerides; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Glycerides, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(C8-10; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Sunscreens
(UV blockers; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Soaps
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(alkali metal; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Phosphates, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkyl; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Quaternary ammonium compounds, uses
RL: NUU (Nonbiological use, unclassified); USES (Uses)
(alkylbenzyldimethyl, chlorides, preservative; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Essential oils
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anise; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Essential oils
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bergamot; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Polymers, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(block; lipid particles on the basis of mixts. of liq. and solid lipids

and method for producing same for drug delivery)
IT UV radiation
(blockers; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)
IT Flow
(boundary-layer; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)
IT Drug delivery systems
(capsules; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)
IT Drug delivery systems
(carriers; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)
IT Hydrocarbons, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chloro; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)
IT Essential oils
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cinnamon; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)
IT Essential oils
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(citrus; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)
IT Essential oils
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clove; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)
IT Aggregates
(coacervates; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)
IT Imaging agents
(contrast; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)
IT Digestive tract
Skin
(cyclosporin delivery to; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)
IT Polyoxyalkylenes, uses
RL: NUU (Nonbiological use, unclassified); USES (Uses)
(dispersion medium; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)
IT Essential oils
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(eucalyptus; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)
IT Drug delivery systems
(fast-dissolving; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)
IT Alcohols, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fatty, branched-chain; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)
IT Alcohols, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(fatty; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)
IT Drug delivery systems

(granules; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Mixers (processing apparatus)
(high-speed; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Diglycerides
Glycerides, biological studies
Monoglycerides
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrogenated coco monoglycerides, diglycerides and triglycerides; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Flocculation
(inhibitors; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Essential oils
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(jasmine; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Diffractometry
(laser; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Essential oils
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lavender; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Essential oils
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lemon; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Antioxidants
Beeswax
Crystallinity
Disperse systems
Drugs
Dyes
Extrusion, nonbiological
Fluorescent dyes
Freeze drying
Homogenization
Lipophilicity
Liquid crystals
Melting point
Particle size distribution
Perfumes
Preservatives
Relaxation
Repellents
Stabilizing agents
Surfactants
Thickening agents
Viscosity
(lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Bentonite, biological studies
Essential oils
Pheromones, animal
Pyrethrins
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Amino acids, biological studies
Corn oil
Lecithins
Olive oil
Phosphatidylglycerols
Phospholipids, biological studies
Quaternary ammonium compounds, biological studies
Sterols
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT **Alditols**
Apolipoproteins
Carnauba wax
Castor oil
Cottonseed oil
Diglycerides
Glycerides, biological studies
Hormones, animal, biological studies
Hydrocarbons, biological studies
Lipids, biological studies
Lipopeptides
Monoglycerides
Paraffin waxes, biological studies
Peanut oil
Peptides, biological studies
Proteins, specific or class
Safflower oil
Soybean oil
Waxes
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Drug delivery systems
(lotions; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Tomography
(magnetic resonance; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Fluidization
(microfluidization; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Essential oils
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mint, Mentha; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Drug delivery systems
(ointments; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Essential oils
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(orange, sweet; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Drug delivery systems
(**parenterals**; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Drug delivery systems
(particles; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Drug delivery systems
(**pellets**; lipid particles on the basis of mixts. of liq. and

solid lipids and method for producing same for drug delivery)

IT Essential oils
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peppermint; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Essential oils
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rose; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Essential oils
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rosemary; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Drug delivery systems
(sachets; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Essential oils
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sandalwood; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Alkali metal salts
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(soaps; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Gelatins, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(soft capsules; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Drying
(spray; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT **Carbohydrates**, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(sugar esters; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Drug delivery systems
(suspensions; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Drug delivery systems
(tablets; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Drug delivery systems
(topical; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT Essential oils
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ylang-ylang; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT 75621-03-3, Chaps 82473-24-3, Chapso
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antiflocculant; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT 994-36-5, Sodium citrate 7722-88-5 14933-08-5, N-Dodecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate
RL: NUU (Nonbiological use, unclassified); USES (Uses)

(antiflocculant; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT 7631-86-9, Silica, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(colloidal; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT 7732-18-5, Water, uses 25322-68-3
RL: NUU (Nonbiological use, unclassified); USES (Uses)
(dispersion medium; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT 50-21-5D, Lactic acid, esters 55-38-9, Fenthion 56-38-2 58-89-9, .gamma.-Hexachlorocyclohexane 62-73-7 76-22-2, Camphor 77-92-9D, Citric acid, esters 80-56-8, .alpha.-Pinene 84-74-2, Dibutylphthalate 87-69-4D, Tartaric acid, esters 94-96-2, 2-Ethyl-1,3-hexanediol 97-53-0, Eugenol 131-11-3, Dimethylphthalate 134-62-3, Deet 138-86-3 311-45-5, Paraoxon 470-82-6, 1,8-Cineol 1490-04-6, Menthol 2451-01-6, Terpinhydrate 9000-07-1, Carrageenan 16752-77-5, Methomyl 22781-23-3, Bendiocarb 34681-23-7 55840-13-6, Glycerol stearate citrate
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT 57-88-5, Cholesterol, biological studies 83-48-7, Stigmasterol 112-92-5, Stearyl alcohol 145-42-6, Sodium taurocholate 149-91-7D, Gallic acid, salts 302-95-4, Sodium deoxycholate 361-09-1, Sodium cholate 863-57-0, Sodium glycocholate 3614-36-6, Diacetyl phosphate 4696-56-4 26658-88-8, Span 36653-82-4, Cetyl alcohol 214353-26-1, Nivea visage
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT 7757-81-5, Sodium sorbate
RL: NUU (Nonbiological use, unclassified); USES (Uses)
(lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT 64-17-5, Ethanol, biological studies 67-63-0, Isopropanol, biological studies 67-68-5, Dmso, biological studies 110-27-0, Isopropylmyristate 538-24-9, Glycerol trilaurate 540-10-3, Cetyl palmitate 1309-38-2, Magnetite, biological studies 7440-26-8D, Technetium, isotopes, biological studies 7440-74-6D, Indium, isotopes, biological studies 7553-56-2D, Iodine, isotopes, biological studies 9005-63-4D, fatty acid esters 9005-65-6, Tween 80 11099-07-3, Glycerol stearate 11140-02-6, Glycerol myristate 11140-06-0, Glycerol palmitate 13463-67-7, Titanium dioxide, biological studies 25168-73-4, **Sucrose** monostearate 25637-97-2, **Sucrose** dipalmitate 27195-16-0, **Sucrose** distearate 29063-28-3, Octanol 35296-72-1, Butanol 37266-93-6, **Sucrose** laurate 37318-31-3, **Sucrose** stearate 42922-74-7, **Sucrose** octanoate 52683-61-1, **Sucrose** oleate 77538-19-3, Glycerol behenate 79217-60-0, Cyclosporin 106392-12-5, Poloxamer 110617-70-4, Poloxamine
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT 1332-37-2, Iron oxide, biological studies 2321-07-5, Fluorescein 3118-97-6, Sudan red 7385-67-3, Nile red
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT 122-18-9, Benzyldimethylhexadecyl ammonium chloride 123-03-5, Cetylpyridinium chloride 25155-18-4, Methylbenzethonium chloride
RL: NUU (Nonbiological use, unclassified); USES (Uses)

(preservative; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

IT 9000-69-5, Pectin 9002-89-5, Polyvinyl alcohol 9003-01-4, Polyacrylic acid 9003-20-7, Polyvinyl acetate 9003-39-8, Polyvinylpyrrolidone 9004-32-4, Sodium carboxymethylcellulose 9004-34-6D, Cellulose, ethers 9004-62-0, Hydroxyethylcellulose 9004-64-2, Hydroxypropyl cellulose 9004-67-5, Methyl cellulose 9005-32-7, Alginic acid 11138-66-2, Xanthan
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thickening agent; lipid particles on the basis of mixts. of liq. and solid lipids and method for producing same for drug delivery)

L73 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:756507 HCAPLUS
DN 133:325636
TI Dry, moldable drug formulation
IN **Buch-Rasmussen, Thomas; Aasmul, Soren; Poulsen, Jens-Ulrik; Flink, James M.; Hansen, Philip; Juul-Mortensen, Claus**
PA Novo Nordisk A/S, Den.
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K009-14
CC **63-6 (Pharmaceuticals)**
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000062759	A1	20001026	WO 2000-DK184	20000413 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI DK 1999-514 A 19990416 <--
AB The present invention relates to a solid pharmaceutical compn. for **parenteral injection** comprising a **binder** and at least one therapeutic agent, said **binder** constituting at least 0.5 % by wt. of the compn. and said **binder** comprising at least one **binding** agent being a **carbohydrate**, and optionally at least one non-crystn. agent, whereby said **binder** forms an **amorphous** matrix, and the amt. of said therapeutic agent consisting of at least one dosage. The pharmaceutical compn. has the strength to be **injected** directly with the need of using cannulas or the like. The therapeutic agent may be any pharmaceutical suitable for **injection**, such as s.c. or i.m. **injection** . A compn. comprising 100% C*Maltidex H16323 (88% **maltitol**) was prepd.
ST drug dry moldable formulation **carbohydrate**
IT Compressive strength
Glass transition temperature
(dry, moldable drug formulation)
IT Antibodies
Carbohydrates, biological studies
Hormones, animal, biological studies
Lipids, biological studies
Nucleic acids
Nucleotides, biological studies
Oligonucleotides
Oligosaccharides, biological studies

Polysaccharides, biological studies
Proteins, general, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dry, moldable drug formulation)
IT Peptides, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mimetics; dry, moldable drug formulation)
IT **Drug delivery systems**
(**parenterals**; dry, moldable drug formulation)
IT **Drug delivery systems**
(**pellets**; dry, moldable drug formulation)
IT **50-70-4**, **Sorbitol**, biological studies **50-99-7**, **Glucose**, biological studies **57-48-7**, **Fructose**, biological studies **57-50-1**, **Sucrose**, biological studies **63-42-3**, **Lactose 69-65-8**, **Mannitol 69-79-4**, **Maltose 87-79-6**, **Sorbose 99-20-7**, **Trehalose 470-55-3**, **Stachyose 512-69-6**, **Raffinose 528-50-7**, **Cellobiose 534-46-3**, **Sophorose 547-25-1**, **Turanose 585-88-6**, **Maltitol 585-99-9**, **Melibiose 597-12-6**, **Melezitose 3458-28-4**, **Mannose 4618-18-2**, **Lactulose 9004-54-0**, **Dextran**, biological studies **13718-94-0**, **Isomaltulose 17606-72-3**, **Maltulose**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dry, moldable drug formulation)
RE.CNT 3
RE
(1) Bukh Meditec AS; WO 9422423 A1 1994 HCAPLUS
(2) Quadrant Holdings Cambridge Limited; WO 9603978 A1 1996 HCAPLUS on IDS
(3) Quadrant Holdings Cambridge Limited; WO 9933853 A2 1999 HCAPLUS

L73 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:553423 HCAPLUS
DN 133:155406
TI Delivery system and methods for **gene therapy**
IN Platt, David; Chang, Yan
PA Safescience, Inc., USA
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-715
ICS C12N015-00; C12N015-63; C12N015-85
CC **63-5** (**Pharmaceuticals**)
Section cross-reference(s): 3
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000045825	A1	20000810	WO 2000-US2628	20000202
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 1999-118244	P	19990202		
	US 2000-495675	A	20000201		

AB According to the present invention, there is provided a gene therapy material which includes a nucleic acid material and a **carbohydrate** wherein the **carbohydrate** preferably is a modified pectin. Also in accordance with the present invention, there is provided a gene therapy

material including a nucleic acid material, a **carbohydrate** material assocd. with the nucleic acid material, and a protective coating disposed about the **carbohydrate** material. Also in accordance with the present invention, there is provided a method for treating a tumor of the type which has **carbohydrate binding** sites expressed on the surface thereof by providing a therapeutic material, incorporating the therapeutic material into a body of a modified pectin material so as to produce a therapeutic compn., and administering the therapeutic compn. to a patient.

ST gene delivery therapy **carbohydrate** antitumor

IT Gene, animal
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(cytosine deaminase-encoding; delivery system and methods for gene therapy)

IT Antitumor agents
Drug delivery systems
Drug targeting
Gene therapy
Genetic vectors
Neoplasm
Plasmid vectors
Retroviral vectors
Virus vectors
(delivery system and methods for gene therapy)

IT **Carbohydrates**, biological studies
DNA
Nucleic acids
RNA
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(delivery system and methods for gene therapy)

IT Neoplasm
(gene delivery to; delivery system and methods for gene therapy)

IT Apoptosis
(genes promoting; delivery system and methods for gene therapy)

IT **Drug delivery systems**
(**injections**; delivery system and methods for gene therapy)

IT **Drug delivery systems**
(liposomes; delivery system and methods for gene therapy)

IT Encapsulation
(microencapsulation; delivery system and methods for gene therapy)

IT **Drug delivery systems**
(**parenterals**; delivery system and methods for gene therapy)

IT Gene, animal
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(tumor suppressor; delivery system and methods for gene therapy)

IT Adeno-associated virus
Adenoviridae
Baculoviridae
Cosmids
DNA viruses
Phagemids
RNA viruses
(vectors; delivery system and methods for gene therapy)

IT 9000-69-5D, Pectins, derivs.
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(delivery system and methods for gene therapy)

IT 9025-05-2, Cytosine deaminase 86090-08-6, Angiostatin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene encoding; delivery system and methods for gene therapy)

IT 1398-61-4, Chitin 9012-76-4, Chitosan
RL: PEP (Physical, engineering or chemical process); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study);

PROC (Process); USES (Uses)
(particle coating; delivery system and methods for gene therapy)
RE.CNT 7
RE
(1) Crystal; Hum Gene Ther 1997, V8, P985 HCAPLUS
(2) Leong; J Control Release 1998, V53, P183 HCAPLUS
(3) Pienta; J Natl Cancer Inst 1995, V87(5), P348 HCAPLUS
(4) Raz; US 5895784 A 1999 HCAPLUS
(5) Roy; US 5972707 A 1999 HCAPLUS
(6) Tanaka; Cancer Res 1998, V58, P3362 HCAPLUS
(7) Xu; Hum Gene Ther 1997, V8, P177 HCAPLUS

L73 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:456857 HCAPLUS
DN 133:94495
TI **Polyol**/oil suspensions for the **sustained release** of proteins
IN Goldenberg, Merrill Seymour; Shan, Daxian; Beekman, Alice C.
PA Amgen Inc., USA
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K009-10
ICS A61K047-00; A61K047-26; A61K047-12; A61K047-44; A61K047-10
CC **63-5** (**Pharmaceuticals**)
Section cross-reference(s): 2, 15
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000038652	A1	20000706	WO 1999-US30527	19991220
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6245740	B1	20010612	US 1998-221181	19981223
PRAI	US 1998-221181	A	19981223		
	US 1999-448205	A	19991123		

AB The present invention relates to the prepn. of **polyol**/thickened oil suspensions contg. a biol. active agent, for the sustained delivery of the biol. active agent. The described protein/glycerol/oil suspensions show sustained release of protein, e.g., granulocyte-colony stimulating factor (G-CSF), of up to at least one week.
ST **polyol** oil suspension protein sustained release
IT Glycoproteins, specific or class
RL: BPR (Biological process); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(TNF-BP (tumor necrosis factor-**binding** protein); **polyol**/oil suspensions for the sustained release of proteins)
IT Neurotrophic factors
RL: BPR (Biological process); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(brain-derived; **polyol**/oil suspensions for the sustained release of proteins)
IT Proteins, specific or class
RL: BPR (Biological process); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(erythropoiesis-stimulating; **polyol**/oil suspensions for the

sustained release of proteins)
IT Neurotrophic factors
RL: BPR (Biological process); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(glial-derived; **polyol**/oil suspensions for the sustained release of proteins)
IT **Drug delivery systems**
(**injections**, i.m.; **polyol**/oil suspensions for the sustained release of proteins)
IT **Drug delivery systems**
(**injections**, s.c.; **polyol**/oil suspensions for the sustained release of proteins)
IT Saffron (Crocus sativus)
(oil; **polyol**/oil suspensions for the sustained release of proteins)
IT Liquids
(oils; **polyol**/oil suspensions for the sustained release of proteins)
IT Salts, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(org.; **polyol**/oil suspensions for the sustained release of proteins)
IT **Drug delivery systems**
(**parenterals**; **polyol**/oil suspensions for the sustained release of proteins)
IT Alcohols, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(polyhydric; **polyol**/oil suspensions for the sustained release of proteins)
IT Beeswax
Protein sequences
Syringes
Thickening agents
(**polyol**/oil suspensions for the sustained release of proteins)
IT Interferons
Interleukin 1 receptor antagonist
Proteins, general, biological studies
Stem cell factor
RL: BPR (Biological process); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**polyol**/oil suspensions for the sustained release of proteins)
IT Canola oil
Castor oil
Cottonseed oil
Olive oil
Peanut oil
Sunflower oil
Waxes
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**polyol**/oil suspensions for the sustained release of proteins)
IT Fats and Glyceridic oils, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(sesame; **polyol**/oil suspensions for the sustained release of proteins)
IT Drying
(spray; **polyol**/oil suspensions for the sustained release of proteins)

IT **Drug delivery systems**
(suspensions; **polyol**/oil suspensions for the sustained release of proteins)
IT **Drug delivery systems**
(sustained-release; **polyol**/oil suspensions for the sustained release of proteins)
IT 102484-11-7, Colony-stimulating factor, granulocyte (human)
RL: BOC (Biological occurrence); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)
(amino acid sequence; **polyol**/oil suspensions for the sustained release of proteins)
IT 9014-42-0, MGDF
RL: BPR (Biological process); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(megakaryocyte derived growth factor; **polyol**/oil suspensions for the sustained release of proteins)
IT 11096-26-7, Erythropoietin 83869-56-1, Gmcsf 130939-66-1, Neurotrophic factor 3 143011-72-7, Gcsf 148348-15-6, Fibroblast growth factor 7 169494-85-3, Leptin 205944-50-9, Osteoprotegerin
RL: BPR (Biological process); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**polyol**/oil suspensions for the sustained release of proteins)
IT 50-69-1, Ribose 56-81-5, Glycerol, biological studies **57-48-7, Fructose**, biological studies **57-50-1, Sucrose**, biological studies 58-86-6, Xylose, biological studies 59-02-9, .alpha.-Tocopherol 59-23-4, Galactose, biological studies **69-79-4, Maltose** 87-89-8, Inositol 111-62-6, Ethyl oleate 147-81-9, Arabinose 149-32-6, Erythritol
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**polyol**/oil suspensions for the sustained release of proteins)
IT 7047-84-9, Aluminum monostearate
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(thickener; **polyol**/oil suspensions for the sustained release of proteins)
RE.CNT 5
RE
(1) Beecham Group Plc; EP 0389177 A 1990 HCAPLUS
(2) Mitchell, J; US 5411951 A 1995 HCAPLUS
(3) Monsanto Co; EP 0374120 A 1990 HCAPLUS
(4) Schering Corp; WO 9618417 A 1996 HCAPLUS
(5) Univ Minnesota; WO 8502118 A 1985 HCAPLUS

L73 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:351393 HCAPLUS
DN 132:352833
TI Stable **amorphous** amifostine compositions and methods for the preparation and use of same
IN Stogniew, Martin; Zadei, Javad M.
PA U.S. Bioscience, Inc., USA
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K047-18
ICS A61K031-66; A61K009-19
CC **63-6** (Pharmaceuticals)
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2000029025 A1 20000525 WO 1999-US27050 19991115
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1998-192933 A 19981116
AB The present invention relates to sterile, stable dosage forms suitable for reconstitution and **parenteral** administration to a patient, the dosage form comprising an **amorphous** aminoalkyl dihydrogen phosphorothioate, amifostine in particular. The invention further relates to a method of prepg. such a dosage form, which typically exhibits enhanced thermal stability as compared to existing vacuum dried **amorphous** amifostine. An aq. soln. was formulated contg. amifostine 100 and nicotinamide 12.5 mg/mL and transferred to vials, which were subjected to freeze-drying process. This procedure resulted in thermally-stable single dose vials contg. .apprx.500 mg amifostine and 62.5 mg nicotinamide stabilizer as an elegant cake.
ST freeze dried amifostine amino acid stabilizer; nicotinamide stabilizer amifostine lyophilizate **parenteral** administration
IT Amides, biological studies
Amino acids, biological studies
Gelatins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(freeze-dried compns. contg. **amorphous** amifostine and stabilizers for reconstitution and **parenteral** administration)
IT Drug delivery systems
(**parenterals**, freeze-dried; freeze-dried compns. contg. **amorphous** amifostine and stabilizers for reconstitution and **parenteral** administration)
IT 31098-42-7P, 2-[(3-Aminopropyl)amino]ethanethiol
RL: BYP (Byproduct); PREP (Preparation)
(freeze-dried compns. contg. **amorphous** amifostine and stabilizers for reconstitution and **parenteral** administration)
IT **50-70-4**, **Sorbitol**, biological studies **50-99-7**, Dextrose, biological studies 56-40-6, Glycine, biological studies 56-41-7, Alanine, biological studies **57-50-1**, **Sucrose**, biological studies 59-67-6, Nicotinic acid, biological studies 60-00-4, Ethylenediaminetetraacetic acid, biological studies 61-90-5, Leucine, biological studies 63-91-2, Phenylalanine, biological studies 67-43-6, Diethylenetriaminepentaacetic acid **69-65-8**, **Mannitol** 70-47-3, Asparagine, biological studies 72-18-4, Valine, biological studies 73-22-3, Tryptophan, biological studies 73-32-5, Isoleucine, biological studies 77-92-9, Citric acid, biological studies 87-69-4, Tartaric acid 87-89-8, Inositol 98-92-0, Nicotinamide 145-42-6, Sodium taurocholate 302-95-4, Sodium deoxycholate 7647-14-5, Sodium chloride, biological studies 9004-32-4, Sodiumcarboxymethyl cellulose **9004-54-0**, **Dextran**, biological studies 20537-88-6, Amifostine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(freeze-dried compns. contg. **amorphous** amifostine and stabilizers for reconstitution and **parenteral** administration)
RE.CNT 4
RE
(1) Jahansouz, H; PHARMACEUTICAL RESEARCH 1991, V7(9 SUPPL), PS195
(2) US Bioscience; WO 9403179 A 1994 HCAPLUS
(3) US Bioscience; WO 9834622 A 1998 HCAPLUS
(4) Zadeii, J; PHARMACEUTICAL RESEARCH 1991, V8(10 Suppl), PS172

L73 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:595003 HCAPLUS

DN 131:219191
TI Polynucleotide composition, method of preparation, and use thereof
IN Musunuri, Shankar; Deluca, Patrick P.
PA American Home Products Corporation, USA
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K048-00
ICS C07H001-08
CC **63-6** (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9945966	A1	19990916	WO 1999-US5547	19990312
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9930868	A1	19990927	AU 1999-30868	19990312
BR 9908754	A	20001128	BR 1999-8754	19990312
EP 1061955	A1	20001227	EP 1999-912502	19990312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1998-78080 P 19980313
WO 1999-US5547 W 19990312

AB A lyophilized polynucleotide compn. contains at least one polynucleotide and at least one cryoprotectant, wherein the ratio of the polynucleotide to cryoprotectant is from about 0.001 to about 1.0 part by wt. polynucleotide per 1.0 part by wt. of the cryoprotectant. This compn. also contains from about 0.5 wt. percent to about 6 wt. percent water, based on the total wt. of the final lyophilized polynucleotide compn. The polynucleotide compn. of this invention is characterized by enhanced stability, in that it retains at least 90 % supercoil over a time period of at least 10 days at a temp. of about 37 >C. The lyophilized polynucleotide compn. also has improved soly. An improved process for lyophilization of polynucleotides employs a specific primary drying cycle, that results in the above-described stable, lyophilized polynucleotide compn.

ST freeze dried polynucleotide cryoprotectant
IT Plasmids
(24; lyophilized polynucleotide compn., method of prepn., and use thereof)
IT Conformation
(A form; lyophilized polynucleotide compn., method of prepn., and use thereof)
IT Conformation
(B form; lyophilized polynucleotide compn., method of prepn., and use thereof)
IT Conformation
(Z form; lyophilized polynucleotide compn., method of prepn., and use thereof)
IT **Carbohydrates**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(acidic, cryoprotectants; lyophilized polynucleotide compn., method of prepn., and use thereof)
IT **Carbohydrates**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(aldonic acids, cryoprotectants; lyophilized polynucleotide compn.,

method of prepn., and use thereof)
IT **Carbohydrates**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(aldoses, cryoprotectants; lyophilized polynucleotide compn., method of prepn., and use thereof)
IT **Carbohydrates**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(amino sugars, cryoprotectants; lyophilized polynucleotide compn., method of prepn., and use thereof)
IT Drug delivery systems
(carriers; lyophilized polynucleotide compn., method of prepn., and use thereof)
IT Polyoxyalkylenes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cryoprotectant; lyophilized polynucleotide compn., method of prepn., and use thereof)
IT **Alditols**
Disaccharides
Polysaccharides, biological studies
Uronic acids
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cryoprotectants; lyophilized polynucleotide compn., method of prepn., and use thereof)
IT Drug delivery systems
(freeze-dried; lyophilized polynucleotide compn., method of prepn., and use thereof)
IT Drug delivery systems
(intrapulmonary; lyophilized polynucleotide compn., method of prepn., and use thereof)
IT **Carbohydrates**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(ketoses, cryoprotectants; lyophilized polynucleotide compn., method of prepn., and use thereof)
IT **Amorphous** structure
Buffers
Cryoprotectants
Supercoiled structure
Virus vectors
(lyophilized polynucleotide compn., method of prepn., and use thereof)
IT DNA
RNA
mRNA
tRNA
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lyophilized polynucleotide compn., method of prepn., and use thereof)
IT Polynucleotides
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lyophilized polynucleotide compn., method of prepn., and use thereof)
IT Drug delivery systems
(nasal; lyophilized polynucleotide compn., method of prepn., and use thereof)
IT Drug delivery systems
(oral; lyophilized polynucleotide compn., method of prepn., and use thereof)
IT Drug delivery systems
(**parenterals**; lyophilized polynucleotide compn., method of prepn., and use thereof)
IT **50-70-4**, **Sorbitol**, biological studies **50-99-7**, **Glucose**, biological studies **57-50-1**, **Sucrose**,

biological studies **63-42-3, Lactose 69-65-8, Mannitol** 87-89-8, Inositol **99-20-7, Trehalose** 25322-68-3
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cryoprotectant; lyophilized polynucleotide compn., method of prepn., and use thereof)
IT 7732-18-5, Water, biological studies
RL: BOC (Biological occurrence); REM (Removal or disposal); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(lyophilized polynucleotide compn., method of prepn., and use thereof)
RE.CNT 6
RE
(1) Akzo Nobel Nv; WO 9527721 A 1995 HCAPLUS
(2) Cryolife Inc; WO 9300807 A 1993 HCAPLUS
(3) Mark, B; WO 9740839 A 1997 HCAPLUS
(4) Markus, M; WO 9847490 A 1998 HCAPLUS
(5) Univ California; WO 9641873 A 1996 HCAPLUS
(6) Univ Pittsburgh; WO 9627393 A 1996 HCAPLUS

L73 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:31050 HCAPLUS
DN 130:227652
TI Effects of Additives on the Stability of Humicola lanuginosa Lipase during Freeze-Drying and Storage in the Dried Solid
AU Kreilgaard, Lotte; Frokjaer, Sven; **Flink, James M.**; Randolph, Theodore W.; Carpenter, John F.
CS Department of Pharmaceutical Sciences School of Pharmacy, University of Colorado Health Sciences Center, Denver, CO, 80262, USA
SO J. Pharm. Sci. (1999), 88(3), 281-290
CODEN: JPMSAE; ISSN: 0022-3549
PB American Chemical Society
DT Journal
LA English
CC **63-5** (Pharmaceuticals)
AB The effects of various classes of additives on the stability of a protein with a relatively hydrophobic surface, Humicola lanuginosa lipase (HLL), during lyophilization and storage in the dried solid, were investigated. Prior to lyophilization, it was found that 1M **trehalose** or 1% Tween 20 caused the protein to ppt. IR spectroscopy indicated that **trehalose** "salted-out" native HLL, whereas Tween 20 induced non-native aggregates. Optimal recovery of native protein in the initial dried solid was obtained in the presence of additives which formed an amorphous phase and which had the capacity to hydrogen bond to the dried protein (e.g., **trehalose** and **sucrose**). Additives which crystd. during lyophilization (e.g., **mannitol**) or which remained amorphous, but were unable to hydrogen bond to the dried protein (e.g., **dextran**), afforded less stabilization relative to that seen in the absence of additives. Optimal storage stability in the dried solid required that both protein unfolding during lyophilization was minimized and that the formulation was stored at a temp. below its Tg value. Crystn. of **sucrose** during storage greatly reduced the storage stability of HLL. This was attributed to the increased moisture content and the reduced Tg value in the remaining amorphous phase contg. the protein. **Sucrose** crystn. and the resulting damage to the protein were inhibited by decreasing the mass ratio of **sucrose** :protein.
ST additive stability lipase freeze drying storage
IT Crystallization
Freeze drying
Glass transition temperature
(additives effect on stability of lipase during freeze-drying and storage in dried solid)
IT Proteins (general), biological studies
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(additives effect on stability of lipase during freeze-drying and storage in dried solid)
IT 9001-62-1, Lipase
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(Humicola lanuginosa; additives effect on stability of lipase during freeze-drying and storage in dried solid)
IT **57-50-1, Sucrose**, biological studies **69-65-8, D-Mannitol 99-20-7, Trehalose 9004-54-0, Dextran**, biological studies 9005-64-5, Tween 20
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(additives effect on stability of lipase during freeze-drying and storage in dried solid)
RE.CNT 45
RE
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L73 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:797798 HCAPLUS
DN 130:129859

TI Effects of additives on the stability of recombinant human factor XIII during freeze-drying and storage in the dried solid
AU Kreilgaard, Lotte; Frokjaer, Sven; **Flink, James M.**; Randolph, Theodore W.; Carpenter, John F.
CS Department of Pharmaceutics, The Royal Danish School of Pharmacy, Copenhagen, 80262, Den.
SO Arch. Biochem. Biophys. (1998), 360(1), 121-134
CODEN: ABBIA4; ISSN: 0003-9861
PB Academic Press
DT Journal
LA English
CC **63-5** (Pharmaceuticals)
AB Freeze-drying is often used to improve storage stability of therapeutic proteins. In order to obtain a product with optimal storage stability it is important to understand the mechanisms by which solutes protect the protein against freeze-drying-induced stresses and also against damage induced during subsequent storage. The objective of the current study was to examine the importance of various mechanisms proposed to account for acute and long-term storage stability using recombinant human Factor XIII (rFXIII) as a model protein. Initially, for acute stability during freeze-drying, it was found that solutes which formed an amorphous phase stabilized rFXIII to a greater degree than solutes which crystd. during freeze-drying. However, only amorphous solutes which were able to hydrogen bond to the protein, and thus preserve the native protein structure in the dried solid, provided optimal acute stability. Thus, in addn. to forming an amorphous phase, it was also important to possess the ability to hydrogen bond to the protein. Long-term storage stability was optimal in the presence of solutes which formed and maintained amorphous phases with Tg values above the storage temp. and which also preserved the native protein structure during freeze-drying. Solute crystn. during storage compromised storage stability. (c) 1998 Academic Press.
ST additive stability factor XIII freeze drying
IT Aggregation
Conformation
Freeze drying
Glass transition temperature
(additives effect on stability of recombinant human factor XIII during freeze-drying and storage in dried solid)
IT Polyoxyalkylenes, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(additives effect on stability of recombinant human factor XIII during freeze-drying and storage in dried solid)
IT **57-50-1**, **Sucrose**, biological studies **69-65-8**, D-**Mannitol** **99-20-7**, **Trehalose** **9004-54-0**, **Dextran**, biological studies 9005-64-5, Tween 20 25322-68-3, Polyethylene glycol
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(additives effect on stability of recombinant human factor XIII during freeze-drying and storage in dried solid)
IT 9013-56-3, Factor XIII
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(recombinant human; additives effect on stability of recombinant human factor XIII during freeze-drying and storage in dried solid)
RE.CNT 42
RE
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L73 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:672484 HCAPLUS
DN 129:281023
TI Therapeutic powder formulation for pulmonary administration, containing crystalline insulin
IN Jensen, Steen; **Hansen, Philip**
PA Novo Nordisk A/S, Den.
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-28
CC **63-6** (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9842368	A1	19981001	WO 1998-DK108	19980320
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9866119	A1	19981020	AU 1998-66119	19980320
	US 5898028	A	19990427	US 1998-45316	19980320
	EP 971729	A1	20000119	EP 1998-907915	19980320
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,				

SI, LT, LV, FI, RO
PRAI DK 1997-319 19970320
WO 1998-DK108 19980320
AB A therapeutic powder formulation suitable for pulmonary administration comprising particles composed of human insulin or any analog or deriv. thereof and an enhancer which enhances the absorption of insulin in the lower respiratory tract is disclosed. The powder formulation has a better stability profile than powders of essentially the same compn. prepd. by spray drying, freeze-drying, vacuum drying and open drying. A formulation was prepd. from human insulin, ZnCl2, and sodium taurocholate.
ST insulin powder cryst formulation pulmonary
IT Uptake (biological)
(enhancers; powder formulation for pulmonary administration, contg. cryst. insulin)
IT Crystals
Dry powder inhalants (drug delivery systems)
Lung
Surfactants
(powder formulation for pulmonary administration, contg. cryst. insulin)
IT 145-42-6, Sodium taurocholate
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(powder formulation for pulmonary administration, contg. cryst. insulin)
IT **50-70-4, Sorbitol**, biological studies **57-50-1, Sucrose**, biological studies **69-65-8, Mannitol** 87-89-8, Inositol 87-99-0, Xylitol **99-20-7, Trehalose** 108-95-2, Phenol, biological studies **512-69-6, Raffinose** 994-36-5, Sodium citrate 7647-14-5, Sodium chloride, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(powder formulation for pulmonary administration, contg. cryst. insulin)
IT 8049-62-5, Zinc insulin 9004-10-8, Insulin, biological studies 9004-10-8D, Insulin, hexamer, zinc salt
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(powder formulation for pulmonary administration, contg. cryst. insulin)
IT 116094-23-6 133107-64-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(powder formulation for pulmonary administration, contg. cryst. insulin)

L73 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:434955 HCAPLUS
DN 129:127025
TI Water-solid interactions. IV. Influence of moisture sorption on the compaction of film-coated particles
AU Stubberud, Lars; Eriksson, Maria; Kordnejad, Kamran; Graffner, Christina
CS Pharmaceutical RandD, Astra Lakemedel AB, Soedertaelje, SE-151 85, Swed.
SO Pharm. Dev. Technol. (1998), 3(2), 141-151
CODEN: PDTEFS; ISSN: 1083-7450
PB Marcel Dekker, Inc.
DT Journal
LA English
CC **63-5** (Pharmaceuticals)
AB The effect of moisture sorption on the compaction properties of model modified-release (MR) **pellets** coated with Et cellulose/hydroxypropyl cellulose film was studied for the MR **pellets** alone and in binary mixts. with microcryst. cellulose, **lactose** .alpha.-monohydrate, or **lactose** 9% **amorphous**. The in vitro dissoln. rate prior to and after compaction was used as an indirect method of evaluating the effect of

exposing the MR **pellets** to a compaction force. Moisture sorption as well as the glass transition temp. (Tg) by using DSC were detd. as a function of humidity for cast film conditioned at different humidities using a climate test chamber. The compaction properties of **lactose** and microcryst. cellulose were altered by the addn. of MR **pellets**, resulting in a robust tablet mass and a tensile strength of the tablet masses that was less sensitive to moisture. The amt. of moisture sorbed was found to have little influence on the formation of cracks or on the rupturing of film-coated MR **pellets** during compaction. This was probably a result of both the small depression in the Tg for the film system at increasing RH and the robustness of the film chosen. The vol. redn. properties of the tableting excipients were of importance for reducing damage to the film coating. **Lactose** had a higher protective effect on the film-coated MR **pellets** compared to microcryst. cellulose.

ST film coated particle compaction moisture sorption; cellulose coated particle compaction moisture sorption

IT **Pellets** (drug delivery systems)
(controlled release; moisture sorption effect on compaction of film-coated particles)

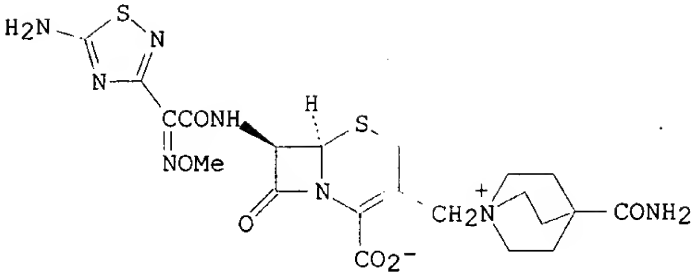
IT Compaction
Density
Dissolution rate
Glass transition temperature
Particle size distribution
Porosity
Relative humidity
Sorption
Surface area
Tablets (drug delivery systems)
Tensile strength
(moisture sorption effect on compaction of film-coated particles)

IT Controlled release drug delivery systems
(**pellets**; moisture sorption effect on compaction of film-coated particles)

IT 9004-34-6, Cellulose, biological studies
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microcryst.; moisture sorption effect on compaction of film-coated particles)

IT **63-42-3, Lactose** 5989-81-1, **Lactose** .alpha.-monohydrate 9004-57-3, Ethyl cellulose 9004-64-2, Hydroxypropyl cellulose
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(moisture sorption effect on compaction of film-coated particles)

L73 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2001 ACS
AN 1990:412018 HCAPLUS
DN 113:12018
TI Solid-state stability and preformulation study of a new **parenteral** cephalosporin antibiotics (E1040)
AU Ashizawa, Kazuhide; Uchikawa, Kiyohiko; Hattori, Teiichi; Ishibashi, Yasuo; Miyake, Yasuo; Sato, Tadasi
CS Tsukuba Res. Lab., Eisai Co., Ltd., Tsukuba, 300-26, Japan
SO Yakugaku Zasshi (1990), 110(3), 191-201
CODEN: YKKZAJ; ISSN: 0031-6903
DT Journal
LA Japanese
CC **63-5** (Pharmaceuticals)
GI



I

AB In designing dosage forms, one major factor controlling their physicochem. properties is solid forms of the drug powder. The method for improving the physicochem. stability of unstable .beta.-lactam antibiotics is very important. E 1040 (I) is a novel **parenteral** 3-betaine type cephalosporin which has a broad antibacterial spectrum and potent activities against Citrobacter freundii, Enterobacter cloacase, and **glucose**-non-fermentative bacteria, including Pseudomonas aeruginosa. The present study was intended to provide the solid-state chem. stability of perenteral sterile dry dosage form of I. The chem. stability differences among the various solid forms, dry **amorphous** , additive freeze-dried **amorphous** solid and cryst. powder, were evaluated as a function of temp. by thermo stress tests. Freeze-dried anhyd. **amorphous** form was the first sterile dry dosage form investigated during the preformulation study. However, this compd. is chem. unstable; a redn. is obsd. in the freeze-dried **amorphous** solid. In order to select the most suitable solid form of I, two methods were used. One was cryst. solid and the other was NaCl additive freeze-dried formulation. Through the expts., the solid-state chem. stabilization can be achieved by these two methods (effect of crystal structure and effect of NaCl additive).

ST antibiotic E1040 stability solid

IT Cryoprotectants
Freeze drying
Amino acids, biological studies
Salts, biological studies
RL: BIOL (Biological study)
(antibiotic E 1040 solid-state stability in relation to)

IT Decomposition
(of antibiotic E 1040, solid state, additives and freeze drying and cryst. state effect on)

IT **50-70-4**, D-Glucitol, biological studies **50-99-7**, **Glucose**, biological studies 56-40-6, Glycine, biological studies 56-41-7, L-Alanine, biological studies 56-45-1, L-Serine, biological studies 56-84-8, L-Aspartic acid, biological studies 56-86-0, L-Glutamic acid, biological studies 56-87-1, L-Lysine, biological studies 56-89-3, L-Cystine, biological studies **57-50-1**, biological studies 60-18-4, L-Tyrosine, biological studies 61-90-5, L-Leucine, biological studies **63-42-3**, **Lactose** 63-68-3, L-Methionine, biological studies **69-65-8**, D-**Mannitol** 71-00-1, L-Histidine, biological studies 72-18-4, L-Valine, biological studies 72-19-5, L-Threonine, biological studies 73-22-3, L-Tryptophan, biological studies 73-32-5, L-Isoleucine, biological studies 74-79-3, L-Arginine, biological studies 77-92-9, biological studies 87-69-4, biological studies 87-99-0, Xylitol 110-15-6, Butanedioic acid, biological studies 110-16-7, 2-Butenedioic acid (Z)-, biological studies 147-85-3, L-Proline, biological studies 7447-40-7, Potassium chloride, biological studies 7647-01-0, Hydrochloric acid, biological studies 7647-14-5, Sodium chloride, biological studies 7664-93-9, Sulfuric acid, biological studies 10043-52-4, Calcium chloride (CaCl2), biological studies 15595-35-4
RL: BIOL (Biological study)
(antibiotic E 1040 solid-state stability in relation to)

IT 105239-91-6
RL: BIOL (Biological study)
(solid-state stability of, formulation in relation to)

L73 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2001 ACS
AN 1989:639517 HCAPLUS
DN 111:239517
TI Transmucosal delivery formulations containing polypeptides
IN Sorensen, Anders Robert; Engesgaard, Anne; **Hansen, Philip Edgar**
PA Novo Industri A/S, Den.
SO Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM A61K047-00
ICS A61K037-24
CC **63-6** (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 308181	A1	19890322	EP 1988-308460	19880913
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	ZA 8806775	A	19890530	ZA 1988-6775	19880912
	DD 282396	A5	19900912	DD 1988-319744	19880913
	WO 8902279	A1	19890323	WO 1988-DK151	19880914
	W: AU, DK, FI, HU, JP, KR, NO, SU, US				
	CN 1031940	A	19890329	CN 1988-106763	19880914
	AU 8824816	A1	19890417	AU 1988-24816	19880914
	HU 53281	A2	19901028	HU 1988-5826	19880914
	CS 274435	B2	19910411	CS 1988-6143	19880914
	JP 03502920	T2	19910704	JP 1988-507564	19880914
	NO 9001161	A	19900313	NO 1990-1161	19900313
	DK 9000667	A	19900314	DK 1990-667	19900314
PRAI	DK 1987-4774		19870914		
	DK 1987-6825		19871223		
	WO 1988-DK151		19880914		

AB The transmucosal delivery of pharmacol. active polypeptides is enhanced by a monosaccharide or an oligosaccharide. Human insulin (4.56 mg) was ground in a mortar with 395.47 mg .alpha.-cyclodextrin to give a powder with an insulin content of 0.3 IU/mg. The hypoglycemic effect of the powder was tested with rabbit after administration as nasal spray.

ST mucosa polypeptide absorption enhancer saccharide; insulin cyclodextrin powder nasal spray

IT Mucous membrane
(polypeptide drug administration through, saccharide absorption enhancers for)

IT Peptides, biological studies
RL: BIOL (Biological study)
(therapeutic, transmucosal compns. contg., saccharide absorption enhancers in)

IT **Monosaccharides**
Oligosaccharides
RL: BIOL (Biological study)
(transmucosal absorption enhancers, for polypeptide drugs)

IT Pharmaceutical dosage forms
(mucosal, contg. insulin, saccharides in, as absorption enhancers)

IT Pharmaceutical dosage forms
(powders, nasal, contg. insulin, saccharides in, as absorption enhancers)

IT 50-69-1, D-Ribose 58-86-6, D-Xylose, biological studies **87-79-6**, L-**Sorbose** 488-84-6, D-erythro-2-Pentulose 583-50-6 1114-34-7, D-Lyxose 3019-74-7, D-Sedoheptulose **3458-28-4**, D-**Mannose** 4300-28-1, D-Ribose 5-phosphate 5328-37-0, L-Arabinose 7585-39-9, .beta.-Cyclodextrin 10016-20-3, .alpha.-Cyclodextrin 17465-86-0, .gamma.-Cyclodextrin
RL: BIOL (Biological study)

(transmucosal absorption enhancer, for polypeptide drugs)
IT **69-79-4D**, ethers with cyclodextrins 12619-70-4D, Cyclodextrin, maltosyl ethers
RL: BIOL (Biological study)
(transmucosal absorption enhancers, for polypeptide drugs)
IT 9004-10-8, Insulin, biological studies 9007-92-5, Glucagon, biological studies
RL: BIOL (Biological study)
(transmucosal compn. contg., saccharide absorption enhancers in)

L73 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2001 ACS
AN 1989:63752 HCAPLUS
DN 110:63752
TI Nasal formulations containing phospholipid absorption enhancers
IN **Hansen, Philip Edgar**; Sorensen, Anders Robert
PA Novo Industri A/S, Den.
SO Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM A61K009-06
ICS A61K047-00
CC **63-6** (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 272097	A2	19880622	EP 1987-311054	19871215
	EP 272097	A3	19880824		
	EP 272097	B1	19920805		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	ZA 8709284	A	19880831	ZA 1987-9284	19871210
	WO 8804556	A1	19880630	WO 1987-DK158	19871215
	W: AU, DK, FI, HU, JP, KR, NO, SU, US				
	AU 8810858	A1	19880715	AU 1988-10858	19871215
	AU 606121	B2	19910131		
	DD 265800	A5	19890315	DD 1987-310485	19871215
	JP 01501550	T2	19890601	JP 1988-501126	19871215
	JP 07068149	B4	19950726		
	HU 57592	A2	19911230	HU 1988-642	19871215
	HU 209247	B	19940428		
	AT 79039	E	19920815	AT 1987-311054	19871215
	ES 2044957	T3	19940116	ES 1987-311054	19871215
	JP 07068149	B4	19950726	JP 1987-501126	19871215
	CN 87108340	A	19880713	CN 1987-108340	19871216
	CN 1034105	B	19970226		
	CS 273139	B1	19910312	CS 1987-9304	19871216
	CA 1326210	A1	19940118	CA 1987-554555	19871216
	DK 8804556	A	19880815	DK 1988-4556	19880815
	FI 8803783	A	19880815	FI 1988-3783	19880815
	FI 94024	B	19950331		
	FI 94024	C	19950710		
	NO 8803627	A	19880815	NO 1988-3627	19880815
	NO 175566	B	19940725		
	NO 175566	C	19941102		
	SU 1837869	A3	19930830	SU 1988-4356382	19880815
	US 5179079	A	19930112	US 1991-819141	19911127
PRAI	DK 1986-6042		19861216		
	DK 1987-3700		19870716		
	EP 1987-311054		19871215		
	WO 1987-DK158		19871215		
	US 1988-172409		19880324		

OS MARPAT 110:63752
AB Prepns. for intranasal administration contain a pharmaceutically active agent and an absorption enhancing system contg. .gtoreq.1 phospholipid R1OCH2CH(OR2)CHOP(O)(OH)(OR3) (R1, R2 = H, C1-14 alkyl, alkenyl, alkylcarbonyl, alkenylcarbonyl; R1 and R2 are not both H; R3 =

Me3N+CH2CH2, H2NCH2CH2, 2-carboxy-2-aminoethyl, 2,3-dihydroxypropyl, 2,3,4,5,6-pentahydroxycyclohexyl). Human insulin (722 mg), 40 mL 0.02M aq. HCl, 1.6 g glycerol, and water were mixed and the pH was adjusted to 7.4. Didecanoyl-L-phosphatidylcholine (I) (1.0 g) was dissolved in 2 mL EtOH, the soln. was injected into 10 mL water, and the suspension was ultrasonicated to give a colloid which was added to the insulin soln., and the vol. was adjusted to 100 mL. This prepn. (100 mL) (200 I.U./mL) was administered to the nasal cavity of rabbits. After 30 min, the blood **glucose** was 56% of initial levels, after 60 min, 65, after 90 min 70, and after 120 min 81% of initial levels, whereas rabbits treated with insulin without I showed unchanged blood **glucose**.

ST nose drug penetration enhancer phospholipid

IT Coconut oil
Corn oil
Olive oil
Peanut oil
Soybean oil
Sunflower oil
RL: BIOL (Biological study)
(absorption enhancer contg. phospholipid and, for nasal pharmaceuticals)

IT Phosphatidylethanolamines
Phospholipids, biological studies
RL: BIOL (Biological study)
(absorption enhancers, for nasal administration of polypeptides)

IT Phosphatidylcholines, biological studies
RL: BIOL (Biological study)
(absorption enhancers, for polypeptides in nasal pharmaceuticals)

IT Peptides, biological studies
Proteins, biological studies
RL: BIOL (Biological study)
(therapeutic, intranasal administration of, phospholipid absorption enhancers for)

IT Pharmaceutical dosage forms
(nasal, absorption enhancers for, phospholipids as)

IT Oils, glyceridic
RL: BIOL (Biological study)
(vegetable, absorption enhancer contg. phospholipid and, for nasal pharmaceuticals)

IT 3476-42-4 5655-17-4 13699-45-1 13699-47-3 13699-48-4, Dimyristoyl phosphatidylcholine 92312-23-7, Didecyl-O-phosphatidylcholine
RL: BIOL (Biological study)
(absorption enhancer, for polypeptides in nasal pharmaceuticals)

IT 9004-10-8, Insulin, biological studies 9007-92-5, Glucagon, biological studies
RL: BIOL (Biological study)
(pharmaceuticals contg. phospholipid absorption enhancers and, for nasal administration)

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FILE 'WPIX' ENTERED AT 16:54:54 ON 19 JUL 2001

FILE LAST UPDATED: 16 JUL 2001 <20010716/UP>
MOST RECENT DERWENT UPDATE 200139 <200139/DW>
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SEE http://www.derwent.com/covcodes.html <<<

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L102 ANSWER 1 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-380965 [40] WPIX
CR 2000-376457 [32]
DNC C2001-116630
TI Compositions comprising particles of a solid dispersion comprising antiviral compounds and water-soluble polymers obtained by melt-extrusion, useful for treating viral infections.
DC A96 B02 B03
IN BAERT, L; VERRECK, G
PA (JANC) JANSSEN PHARM NV
CYC 94
PI WO 2001022938 A1 20010405 (200140)* EN 89p A61K009-14 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
ADT WO 2001022938 A1 WO 2000-EP8522 20000831
PRAI EP 1999-203128 19990924
IC ICM **A61K009-14**
ICS A61K031-505; A61K031-53
AB WO 200122938 A UPAB: 20010719
NOVELTY - Compositions comprising particles of a solid dispersion comprising antiviral compounds and water-soluble polymers, obtained by melt-extrusion.
DETAILED DESCRIPTION - A particle consists of a solid dispersion comprising: (a) a compound of formula (IA), (IB) and/or (IC), their N-oxides, salts or isomers and (b) 1 or more pharmaceutically acceptable water-soluble polymers.
In compounds (IA):
Y = CR5 or N;
A = CH, CR4 or N;
n = 0-4;
Q = -NR1R2 or when Y is CR5, Q may also be H;
R1, R2 = H, OH, 1-12C alkyl, 1-12C alkyloxy, 1 12C alkylcarbonyl, 1-12C alkyloxycarbonyl, aryl, NH2, mono- or di(1-12C alkyl)amino, mono- or di(1-12C alkyl)aminocarbonyl, where each 1-12C alkyl is optionally substituted with 1 or 2 T;
T = OH, 1-6C alkyloxy, hydroxy(1-6C)alkyloxy, carboxyl, 1-6C alkyloxycarbonyl, CN, NH2, imino, aminocarbonyl, aminocarbonylamino, mono- or di(1-6C)alkylamino, aryl or Het; or R1+R2 may form pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(1-12C alkyl)amino(1-4C)alkylidene;
R3 = H, aryl, 1-6C alkylcarbonyl, 1-6C alkyl, 1-6C alkyloxycarbonyl, 1-6C alkyl substituted with 1-6C alkyloxycarbonyl;
R4 = OH, halo, 1-6C alkyl, 1-6C alkyloxy, CN, aminocarbonyl, NO2, NH2, trihalomethyl, trihalomethoxy, or when Y is CR5 then R4 may also be 1-6C alkyl substituted with CN or aminocarbonyl;
R5 = H or 1-4C alkyl;
L = -X1-R6 or -X2-Alk-R7; or when Y is CR5 then L may also be 1-10C alkyl optionally substituted with T, 3 10C alkenyl, 3-10C alkynyl or 3-7C cycloalkyl;
R6, R7 = phenyl optionally substituted with 1-5 T'; or when Y is CR5 then R6 and R7 may also be phenyl substituted with 1-5 aminocarbonyl, trihalomethoxy or trihalomethyl; or when Y is N then R6 and R7 may also be indanyl or indolyl, each optionally substituted with 1-5 T';
T' = halo, OH, 1-6C alkyl, 1-6C alkyloxy, 1-6C alkylcarbonyl, 1-6C alkyloxycarbonyl, formyl, CN, NO2, NH2 or CF3;
X1, X2 = -NR3-, -NH-NH-, -N=N-, -O-, -S-, -SO- or SO2-;

Alk = 1-4C alkanediyl; or

T = 3-7C cycloalkyl; or indanyl, indolyl or phenyl each optionally substituted with 1-5 halo, OH, 1-6C alkyl, 1-6C alkyloxy, CN, aminocarbonyl, 1-6C alkyloxycarbonyl, formyl, NO2, NH2, trihalomethyl, trihalomethoxy or 1-6C alkylcarbonyl;

aryl = phenyl optionally substituted with 1-5 halo, 1-6C alkyl, 1-6C alkyloxy, CN, NO2 or CF3;

Het = pyrrolidinyl, piperidinyl, homopiperidinyl, piperazinyl, morpholinyl, tetrahydrofuranyl or tetrahydrothienyl, each optionally substituted with oxo; or pyrrolyl, furanyl, thienyl, pyridyl, pyrimidinyl, pyrazinyl or pyridazinyl, each optionally substituted with OH.

In formula (IB):

-b1=b2-C(R2a)=b3-b4= = -CH=CH C(R2a)=CH-CH=; -N=CH-C(R2a)=CH-CH=; -CH=N-C(R2a)=CH-CH=; N=CH-C(R2a)=N-CH=; -N=CH-C(R2a)=CH-N=; -CH=N-C(R2a)=N-CH=; or -N=N-C(R2a)=CH-CH=;

q = 0-4;

R6 = H, aryl, formyl, 1-6C alkylcarbonyl, 1-6C alkyloxycarbonyl, or 1-6C alkyl optionally substituted with formyl, 1-6C alkyloxycarbonyl, 1-6C alkylcarbonyl;

R2a = CN, aminocarbonyl, mono- or di(methyl)aminocarbonyl, 1-6C alkyl substituted with CN, aminocarbonyl or mono- or di(methyl)aminocarbonyl, 2-6C alkenyl substituted with CN, or 2-6C alkynyl substituted with CN;

R7 = OH, halo, 1-6C alkyl optionally substituted with CN or -C(=O)R8, 3-7C cycloalkyl, 2-6C alkenyl optionally substituted with 1 or more halo or CN, 2-6C alkynyl optionally substituted with 1 or more halo or CN, 1-6C alkyloxy, 1-6C alkyloxycarbonyl, carboxyl, CN, NO2, NH2, mono- or di(1-6C alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, -S(=O)pR8, -NH S(O)pR8, -CO-R8, -NHC(=O)H, -C(=O)NHNH2, -NHC(=O)R8, C(=NH)R8 or a group of formula (i):

A = N, CH or CR8;

B = NH, O, S or NR8;

p = 1 or 2;

R8 = methyl, NH2, mono- or dimethylamino, or polyhalomethyl;

L1 = 1-10C alkyl, 2-10C alkenyl, 2-10C alkynyl, 3-7C cycloalkyl, each optionally substituted by 1 or 2 W; or -X-R9;

W = 3-7C cycloalkyl; indolyl or isoindolyl, each optionally substituted with 1-4 W'; or phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, each optionally substituted with 1-5 R7;

W' = halo, 1-6C alkyl, OH, 1-6C alkyloxy, CN, aminocarbonyl, NO2, NH2, polyhalomethyl, polyhalomethoxy or 1-6C alkylcarbonyl;

R9 = phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, each optionally substituted with 1-5 R7;

X = -NR6-, -NH-NH-, -N=N-, -O-, C(=O) , -CHOH-, -S-, -S(=O)- or -S(=O)2-;

Q1 = H, 1-6C alkyl, halo, polyhalo(1-6C alkyl) or -NR10R11;

R10, R11 = H, OH, 112C alkyl, 1-12C alkyloxy, 1-12C alkylcarbonyl, 1-12C alkoxycarbonyl, aryl, NH2, mono- or di(1-12C alkyl)amino, or mono- or di(1-12C alkyl)aminocarbonyl, where each 1-12C alkyl is optionally substituted with 1 or 2 W; or

R10+R11 = pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(1-12C alkyl)amino(1-4C)alkylidene;

W = OH, 1-6C alkyloxy, hydroxy(16C alkyl)oxy, carboxyl, 1-6C alkyloxycarbonyl, CN, NH2, imino, mono- or di(1-6C alkyl)amino, polyhalomethyl, polyhalomethoxy, polyhalomethylthio, -S(=O)pR8, -NHS(=O)pR8, -NHC(=O)H, C(=O)NHNH2, -NHC(=O)R8, -C(=NH)R8, aryl or Het;

Y1 = OH, halo, 3-7C cycloalkyl, 2-6C alkenyl optionally substituted with 1 or more halo, 2-6C alkynyl, optionally substituted with 1 or more halo, 1-6C alkyl substituted with CN or -C(=O)R8, 1-6C alkyloxy, 1-6C alkyloxycarbonyl, carboxyl, CN, NO2, NH2, mono- or di(1-6C alkyl)amino, polyhalomethyl, polyhalomethoxy, polyhalomethylthio, -S(=O)pR8, -NH-S(=O)pR8, -C(=O)R8, NHC(=O)H, -C(=O)NHNH2, -NHC(=O)R8, -C(=NH)R8 or aryl;

aryl = phenyl optionally substituted with 1-5 halo, 1-6C alkyl, 3-7C cycloalkyl, 1-6C alkyloxy, CN, NO2, polyhalo(1-6C alkyl) or polyhalo(1-6C alkyl)oxy.

In formula (IC):
-a1=a2-a3=a4- = -CH=CH-CH=CH- (a-1); -N=CH-CH=CH-; -N=CH-N=CH-; -N=CH-CH=N-; or -N=N-CH=CH-;
n = 0-5;
R12 = H, aryl, formyl, 1-6C alkylcarbonyl, 1-6C alkyl, 1 6C alkyloxycarbonyl, 1-6C alkyl substituted with formyl, 1-6C alkylcarbonyl or 1-6C alkyloxycarbonyl;
R13 = as defined for R7;
and provided that certain specified compounds are excluded.
For the full definitions, see DEFINITIONS (Full Definitions) field.
INDEPENDENT CLAIMS are included for the following:
(1) dosage forms comprising the particles; and
(2) use of the particles in dosage forms for oral administration once daily in the treatment of viral infections.
USE - As antiviral agents for treating e.g. HIV infection.
ADVANTAGE - By dispersing the active compounds in a carrier by melt-extrusion to obtain a solid dispersion, the bio-availability of the compounds is improved.
Dwg.0/0

FS CPI
FA AB; GI; DCN
MC CPI: A12-V01; B04-A08; B04-A09; B04-A10; B04-C02A; B04-C02B1; B04-C02B2; B04-C02D; B04-C03; B07-D04; B07-D10; B07-D12; B07-D13; B14-A02; B14-A02B1
TECH UPTX: 20010719

TECHNOLOGY FOCUS - POLYMERS - Preferred Polymers: The water-soluble polymer is e.g. an alkylcellulose, hydroxyalkylcellulose, carboxyalkylcellulose or its alkali metal salt, carboxyalkylcellulose ester, starch, pectin, chitin derivative, di-, oligo- or **polysaccharide**, polyacrylic acid, or polyalkylene oxide, preferably hydroxypropyl methylcellulose HPMC 2910 5 mPas. The polymer preferably has apparent viscosity 1-5000 mPas when dissolved at 20degreesC in an aqueous solution at 2% w/v.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The particle size is less than 1500 microm. The solid dispersion is in the form of a solid solution comprising (a) and (b), or in the form of a dispersion where **amorphous** or microcrystalline (a) or **amorphous** or microcrystalline (b) is dispersed evenly in a solid solution comprising (a) and (b).
The wt. ratio of (a):(b) is 1:1 to 1:899.
Preferred Preparation: The particles are obtained by melt extrusion of the components at 20-300degreesC and grinding, and optionally sieving.

L102 ANSWER 2 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-307192 [32] WPIX
DNC C2001-094791
TI **Transdermal** drug delivery system includes drug or therapeutic agent encapsulated in water-soluble **carbohydrate** and suspended in cyanoacrylate ester.
DC A14 A96 B07
IN PELLEGRINI, F C
PA (FELD-I) FELDMAN S·E
CYC 1
PI US 6207193 B1 20010327 (200132)* 6p A61K009-14 <--
ADT US 6207193 B1 US 1999-472280 19991227
PRAI US 1999-472280 19991227
IC ICM **A61K009-14**
AB US 6207193 B UPAB: 20010611
NOVELTY - A transdermal drug delivery system comprises drug or therapeutic agent encapsulated in water-soluble **carbohydrate**. The **carbohydrate**-encapsulated drug or therapeutic agent is suspended in cyanoacrylate ester that is capable of polymerizing upon contact with moisture or skin tissue.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method of preparing the transdermal drug delivery system, by dissolving or

suspending drug or therapeutic agent in molten water-soluble **carbohydrate**; cooling the molten **carbohydrate** to form a glass-like matrix where drug or therapeutic agent is encapsulated; pulverizing the glass-like matrix to obtain finely divided micro-fine particles; and suspending the particles in cyanoacrylate ester.

USE - For delivering drug or therapeutic agent epidermally or transdermally.

ADVANTAGE - The transdermal drug delivery system is effective, and results in a time release of drug or therapeutic agent to body system.

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: A04-D08; A12-V01; B02-Z; B04-C03B; B07-A02B; B10-A07; B12-M02F; B14-A01; B14-A02; B14-A04; B14-C01
TECH UPTX: 20010611

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred System: The system contains 5-26 (preferably 10-20) wt.% drug or therapeutic agent, and optionally includes 5-20 (preferably 10-15) wt.% plasticizer or 20-400 (preferably 50-300) ppm polymerization inhibitor. Preferred Component: The drug or therapeutic agent is antibiotic, antiviral, antifungal, antibacterial, analgesic, or antiseptic. Preferred Properties: The **carbohydrate** -encapsulated drug or therapeutic agent is in the form of finely divided micro-fine particles having a diameter of 5-50 (preferably 10-40) millimicrons. Preferred Ratio: The ratio of encapsulated drug or therapeutic agent to cyanoacrylate ester is 1:2.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The **carbohydrate** is **monosaccharide** (preferably **glucose**, **mannose**, galactose, or **fructose**) or **disaccharide** (preferably **sucrose**, **lactose**, **maltose** land **cellobiose**). The cyanoacrylate ester is of formula H2C=C(CN)-C(O)-OR.
R = 2-12C alkyl, 5-10C alkenyl, optionally substituted phenyl, 2-ethoxyethyl, 3-methoxybutyl, or preferably 2-10C alkyl or its cyclic ionomers
The plasticizer is dioctyl phthalate.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Component: The polymerization inhibitor is sulfur dioxide.

L102 ANSWER 3 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-257426 [26] WPIX
DNC C2001-077460
TI Microspheres for continuous release of active agent, particularly leuprolide, in physiological medium, comprises copolymer of glycolic acid and lactic acid, and active agent homogeneously distributed within **matrix** of polymer body.
DC A96 B04 B07
IN MURTAGH, J; THANOO, B C
PA (OAKW-N) OAKWOOD LAB LLC
CYC 93
PI WO 2001010414 A1 20010215 (200126)* EN 25p A61K009-14 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US VN YU ZA ZW
AU 2000065104 A 20010305 (200130) A61K009-14 <--
ADT WO 2001010414 A1 WO 2000-US21038 20000802; AU 2000065104 A AU 2000-65104 20000802
FDT AU 2000065104 A Based on WO 200110414
PRAI US 1999-366995 19990804
IC ICM **A61K009-14**
ICS A61K009-50; C08G063-08
AB WO 200110414 A UPAB: 20010515

NOVELTY - Microspheres (I) for continuous release of an active agent in a physiological medium comprises: (i) copolymer of glycolic acid and lactic acid; and (ii) active agent homogeneously distributed within matrix of polymer body, where average number and size of active agent in a particular unit area is the same as a second average number and size of the active in a different unit area of (I).

DETAILED DESCRIPTION - Microspheres (I) for continuous release of effective amounts of an active agent in a physiological medium comprises:

(i) a copolymer of glycolic acid and lactic acid;

(ii) an active agent which is homogeneously distributed within a matrix of the polymer body, where an average number and size of the active agent in a particular unit area is substantially the same as a second average number and size of the active in a different unit area of (I). (I) have an average cross-sectional porosity less than 10% of the total cross-sectional area.

INDEPENDENT CLAIMS are also included for the following:

(A) microspheres (I') for continuous release of effective amounts of an active agent in a physiological medium comprising: (a) a homopolymer of lactic acid; and (b) an active agent as in (ii). (I') has an average cross-sectional porosity less than 10% of the total cross-sectional area;

(B) a pharmaceutical composition comprising microspheres for slow continuous release of effective amounts of a water-soluble active agent in an aqueous physiological medium, where the microspheres comprising a poly(lactide-co-glycolide) copolymer. The active agent is a leuprolide drug at 12-20% homogeneously distributed within a matrix of the polymer bodies, where the leuprolide release is predominantly erosion controlled. The erosion control degrades the polymeric leuprolide-containing matrix and releases a continuous effective amount of the leuprolide into the aqueous physiological medium for at least thirty days. Each of the microspheres has a total cross-sectional porosity less than 10% of the total cross-sectional area;

(C) slow release leuprolide microspheres having a cross-sectional porosity of less than 10% prepared by:

(a) forming a dispersed phase comprising a homogeneous solution of a leuprolide drug and a copolymer of lactide and glycolide;

(b) providing a continuous phase in which the dispersed phase will form an emulsion;

(c) continuously introducing dispersed phase into a reactor vessel at dispersed phase feed rate, and continuous phase into the reactor vessel at a continuous phase feed rate, the reactor vessel including means for forming an emulsion, and forming an emulsion of the dispersed phase in the continuous phase;

(d) continuously transporting the emulsion from the reactor vessel to a solvent removal vessel to remove solvent.

USE - As continuous release microspheres for releasing an active agent into a surrounding physiological medium. The active agent includes steroids, diuretics, **carbohydrates**, amino acids, proteins, enzymes, peptide hormones, analgesic agents, antimalarials, antibiotics, antineoplastics, CNS depressants and stimulants, adrenergic agents, cholinergics, sulfonamides, sulfones, folate reductase inhibitors, vitamins, diagnostic agents, chelating agents and anti-infective agents. The active agent is especially leuprolide acetate which is an agonist derivative of leutenizing hormone-releasing hormone (LH-RH, i.e. gonadotropin-releasing hormone) and which controls and regulates both male and female reproduction. Leuprolide acetate may be used as an antineoplastic agent for treating e.g. endometriosis, anemia secondary to leiomyoma, breast neoplasm, prostate neoplasm, endometrial neoplasm and uterine neoplasm. Leuprolide acetate suppresses testosterone levels and offers an alternative to an orchiectomy (surgical removal of the testicles) or estrogen administration (as testosterone promotes the growth of cancerous cells in the prostate).

ADVANTAGE - The microspheres can be produced using a simple, continuous, economic and efficient process which gives a product of uniform characteristics throughout the production cycle (cf. prior art processes which are unable to produce microspheres having identical characteristics at the end of the production run as ones produced at the

beginning and middle of the run). The microspheres have low porosity and are exceptionally uniform in terms of e.g. size and agent load. Due to the low porosity and fine distribution of active agent within the microsphere, the drug release profile during polymer degradation is constant and highly uniform.

5 x 1000 ml Fractions of microsphere suspension produced in a reactor using 8.75 g RG503H (see 'Example'), 1.25 g leuprolide acetate, 45 g CH2Cl2 and 10.7 g MeOH as the dispersed phase, and 5000 ml 0.35% polyvinyl alcohol (PVA) as the continuous phase were collected. The microspheres of each fraction were separated by filtration, freeze dried in bulk and compared. Microscopic analysis showed that the morphology of the microspheres obtained in all five fractions was identical. E.g. Fractions 1-5 had a load (in %) of : 11.17, 11.31, 10.96, 11.05 and 10.99 respectively; bulk density of: 0.40, 0.48, 0.48, 0.47 and 0.48 respectively; and 50% under (in micro m) of: 18.1, 17.4, 17.8, 17.8 and 17.4 respectively. The figures showed that each fraction of microspheres produced throughout the process had excellent consistency.

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: A05-E02; A12-V01; A12-W05; B04-C03D; B04-J07; B12-M10A; B14-D01; B14-H01; B14-N07A
TECH UPTX: 20010515

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Microspheres: (I) and (I') have an average cross-sectional porosity less than 5% of the total cross-sectional area. (I) have an average particle size of 10-40 microm and an active agent load of at least 9 (preferably at least 15) %. (I') have an average particle size of 10-40 microm, and an active agent load of at least 15%. The continuous release of the active agent within the polymer matrix is essentially by polymer degradation. The active agent is continuously released in an effective amount from (I) over a period of at least 30 days. In (I'), the active agent, leuprolide, is continuously released in an effective amount from each microsphere over a period of at least 90 (preferably 120) days. The active agent is water soluble.

TECHNOLOGY FOCUS - POLYMERS - The poly(lactide-co-glycolide) copolymer has a ratio of glycolide to lactide of 1:1 and an average molecular weight of 26000-36000.

L102 ANSWER 4 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-219998 [23] WPIX
DNC C2001-065804
TI Pharmaceutical composition useful for treating hyperlipemia comprises **micronized** fenofibrate, surfactant and cellulose derivative as binder and solubilizing agent.
DC A96 B05
IN CHENEVIER, P; CRIERE, B; SUPLIE, P
PA (ETHI-N) LAB PROD ETHIQUES ETHYPHARM
CYC 94
PI FR 2795961 A1 20010112 (200123)* 26p A61K009-14 <--
WO 2001003693 A1 20010118 (200123) FR A61K031-216
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000062960 A 20010130 (200127) A61K031-216
ADT FR 2795961 A1 FR 1999-8923 19990709; WO 2001003693 A1 WO 2000-FR1971 20000707; AU 2000062960 A AU 2000-62960 20000707
FDT AU 2000062960 A Based on WO 200103693
PRAI FR 1999-8923 19990709
IC ICM **A61K009-14**; A61K031-216
ICS A61K009-16; A61P003-06; A61P007-02
AB FR 2795961 A UPAB: 20010425
NOVELTY - Pharmaceutical composition comprises micronized fenofibrate, a

surfactant and a cellulose derivative that acts as both a binder and a solubilizing agent.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) production of the composition by spraying neutral microgranules with an aqueous suspension containing the surfactant, the cellulose derivative and micronized fenofibrate and

(2) production of the composition by granulating a mixture of the surfactant, the cellulose derivative and micronized fenofibrate with an aqueous wetting solution and drying and screening the granules.

USE - Fenofibrate is useful for treating hyperlipemia, including hypercholesterolemia and hypertriglyceridemia.

ADVANTAGE - The composition dissolves more rapidly and gives improved fenofibrate bioavailability than prior art compositions e.g. Lipanthyl 200M. Microgranules comprising micronized fenofibrate (64.5%), neutral core (21%), HPMC (11.2%) and polysorbate 80 (3.3%) were produced by spraying neutral cores with an aqueous suspension. The percentage dissolution in a stream of 0.1 N sodium lauryl sulfate (8 ml/min) was 73 after 15 minutes and 95 after 30 minutes. The corresponding figures for Lipanthyl 200M were 47.3 and 64.7.

Dwg.0/4

FS CPI
FA AB; DCN
MC CPI: A03-A00A; A12-V01; B04-C02A; B04-C03; **B04-D01**; B05-A01B; B05-B01B; B10-A09A; B10-F02; B12-M11C; B14-D02A2; B14-F06
TECH UPTX: 20010425

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred composition: The cellulose derivative is hydroxypropyl methylcellulose (HPMC) with an apparent viscosity of 2.4-18 (especially 2.4-3.6) cP, and is present in an amount of 2-15 (preferably 5-12) wt.%. The surfactant is polysorbate 80, Montane (RTM) 20 or sodium lauryl sulfate and is present in an amount of 1-10 (preferably 3-5) wt.% based on fenofibrate. The fenofibrate/HPMC weight ratio is 5/1 to 15/1.

The composition also includes excipients e.g. **lactose**, silicone antifoam and/or talc. The fenofibrate has a mean particle size of less than 8 mum. The composition is in the form of powder- or granule-filled capsules.

L102 ANSWER 5 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-210199 [21] WPIX
CR 1995-275286 [36]; 2000-375587 [32]; 2001-210323 [15]; 2001-272749 [25]
DNC C2001-062367
TI A rapidly dissolving pharmaceutical dosage form, for the oral administration of drugs, comprises a drug and a particulate support **matrix** comprising a bulking agent and two polypeptides having predetermined net charges of the same sign.
DC B04 B07
IN ALLEN, L V; WANG, B
PA (OKLA) UNIV OKLAHOMA
CYC 1
PI US 6177104 B1 20010123 (200121)* 17p A61K009-14 <--
ADT US 6177104 B1 CIP of US 1994-187670 19940127, CIP of US 1994-191237 19940203, CIP of US 1995-487268 19950607, US 1998-111124 19980706
FDT US 6177104 B1 CIP of US 5587180, CIP of US 5776491, CIP of US 5807576
PRAI US 1998-111124 19980706; US 1994-187670 19940127; US 1994-191237 19940203; US 1995-487268 19950607
IC ICM **A61K009-14**
ICS A61K047-42
AB US 6177104 B UPAB: 20010607

NOVELTY - A rapidly dissolving pharmaceutical dosage form comprises:

(1) a particulate support matrix comprising:

(i) two polypeptide components having predetermined net charges of the same sign which together comprise 2-35 wt.% of the particulate support matrix; and

(ii) a bulking agent comprising 45-97 wt.% of the particulate support matrix.

DETAILED DESCRIPTION - A rapidly dissolving pharmaceutical dosage form comprises:

(1) a particulate support matrix, which disintegrates in less than 20 seconds when introduced into an aqueous environment, comprising:

(i) a first polypeptide component with a predetermined net charge and a secondary polypeptide component with a predetermined net charge of the same sign as the net charge as the first component (the two components together comprising 2-35 wt.% of the particulate support matrix and the second polypeptide component having a greater solubility in aqueous solution than the first polypeptide component); and

(ii) a bulking agent comprising 45-97 wt.% of the particulate support matrix.

USE - The dosage form is useful for oral administration of drugs, e.g. antihistamines, decongestants or antibiotics.

ADVANTAGE - The dosage form dissolves rapidly in the mouth and is therefore of use in the treatment of geriatric, pediatric or incarcerated patients who will often retain their medication in the oral cavity while pretending to swallow it and patients who have difficulty swallowing tablets or capsules. The foaming associated with effervescent dosage forms (using e.g. sodium bicarbonate and citric acid) which can lead to unpleasant sensations in the mouth is avoided. The tablets are easier for patients to take and may result in long term benefits such as enhanced patient compliance, fewer hospital admissions due to poor compliance and enhanced health and quality of life.

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B04-N02; B04-N04; B07-A02B; B07-D04C; B10-A07; B10-C02; B10-C04C; B10-E04D; B12-M11J
TECH UPTX: 20010418

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The dosage form further comprises an effervescing agent (0-5%, preferably less than 3%), a binding agent and/or a flavoring agent. The support matrix disintegrates in less than 20, preferably 10 (especially 1-6), seconds in aqueous media. The particulate support matrix has a bulk density of 0.03-0.3, preferably 0.03-0.15, g/ml. The first and second polypeptide components together comprise 5-25, preferably 10-20 (especially 12-16), wt.% of the particulate support matrix. The first polypeptide component and the second polypeptide component are present in the ratio 20:1 to 1:100, preferably 5:1 to 1:40, especially 2:1 to 1:25, most especially 1:2 to 1:10 by weight. The bulking agent comprises 70-92, preferably 75-90 (especially 80-85), wt.% of the particulate support matrix. The flavoring agent comprises 0-10, preferably 0.001-0.05, wt.% of the composition and the binding agent comprises 0-20, preferably 0-5, wt.% of the composition.

Preferred Polypeptides: The first and second polypeptide components both have a net negative charge or, preferably, both have a net positive charge. Both polypeptide components comprise a gelatin which has been hydrolyzed or, preferably, the first polypeptide component is a non-hydrolyzed gelatin and the second polypeptide component is a hydrolyzed gelatin. The second polypeptide component has a lower molecular weight than the first polypeptide component.

Preferred Bulking agent: The bulking agent is **mannitol** or **sorbitol.**

L102 ANSWER 6 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-147130 [15] WPIX
DNC C2001-043477
TI Preparation of a therapeutic composition used in drug delivery comprises an organic solvent of a hydrophobically-derivatized **carbohydrate** (HDC),an ion pair complex (IPC) of a hydrophilic therapeutic agent and an ionic substance.
DC B04 B07 D16
IN JACKSON, P
PA (QUAD-N) QUADRANT HOLDINGS CAMBRIDGE LTD
CYC 93
PI WO 2001003673 A1 20010118 (200115)* EN 15p A61K009-16

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2000061666 A 20010130 (200127) A61K009-16

ADT WO 2001003673 A1 WO 2000-GB2661 20000711; AU 2000061666 A AU 2000-61666 20000711

FDT AU 2000061666 A Based on WO 200103673

PRAI GB 1999-16316 19990712

IC ICM A61K009-16
ICS **A61K009-14**; A61K038-28; A61K047-48

AB WO 200103673 A UPAB: 20010317
NOVELTY - Preparation of a therapeutic composition comprises forming a solution in an organic solvent of a hydrophobically-derivatized **carbohydrate** (HDC) and an ion pair complex (IPC) of a hydrophilic therapeutic agent (I) and an ionic substance (II) and drying the solution.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a solid dose composition comprising HDC, (I) and (II); and
(2) a device for pulmonary delivery of (I) where the device comprises a solid dose composition comprising HDC, (I) and (II) in the form of particles of less than 10 micrometers, especially 1-5 micrometers, the composition having a glassy, **amorphous** form and a Tg of above 20 degrees centigrade.
USE - For delivery of drugs.
ADVANTAGE - The HDC allows the potential for controlled release and aids delivery, in particular, to the deep lung. The process for incorporation of HDC in the compositions is efficient.
Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B04-C02; B04-J01; B04-L01; B11-C04; B12-M05; B12-M11G; D05-A01A1; D05-A01B; D05-H10

TECH UPTX: 20010317
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Method: The drying step preferably comprises spray-drying. (II) is a detergent. The method comprises:
(i) mixing (I) in aqueous solution with (II) to form IPC;
(ii) adding a water-immiscible organic solvent to form an organic phase and allowing the IPC to pass into the organic phase;
(iii) separating the organic phase;
(iv) adding the HDC to the organic phase; and
(v) drying the organic solution; or
(i) mixing (I) and (II) in an aqueous medium to form a precipitate;
(ii) dissolving the precipitate and HDC in an organic solvent; and
(iii) drying the solution.
Preferred Composition: The composition is a glassy, **amorphous** composition having a Tg above 20 degrees centigrade and preferably comprises particles of less than 10 micrometers, especially 1-5 micrometers, or micro needles suitable for ballistic delivery. The precipitate preferably optionally isolated prior to step (ii).

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: (I) is a protein, peptide or polynucleotide, preferably an enzyme or hormone, particularly interferons, growth factors, alpha-chymotrypsin interleukins, calcitonin, growth hormones, leuprolide, colony-stimulating factors or DNase, especially insulin. The HDC has a **carbohydrate** backbone and at least one hydroxy group substituted with a less hydrophilic derivative. HDC is preferably **sorbitol** hexacetate, alpha-**glucose** pentaacetate, beta-**glucose** pentaacetate, 1-O-octyl-beta-D-**glucose** tetraacetate, **trehalose** octaacetate, **trehalose** octapropanoate, **sucrose** octaacetate, beta-4',6'-diisobutyroyl hexaacetyl **lactose**, **sucrose** octapropanoate, **cellobiose** octaacetate,

raffinose undecaacetate, **raffinose** undecaacetate, **raffinose** undecapropanoate or **trehalose** 6,6-diisobutyrate hexaacetate.

L102 ANSWER 7 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-006946 [01] WPIX
DNC C2001-001620
TI Solid pharmaceutical compositions for **parenteral injection**, comprising a **binder** and therapeutic agent(s) e.g. insulin, can be **injected** without cannulae and are stable long-term, solid and moldable.
DC B07
IN AASMUL, S; BUCH-RASMUSSEN, T; FLINK, J M; HANSEN, P; JUUL-MORTENSEN, C; POULSEN, J
PA (NOVO) NOVO NORDISK AS
CYC 92
PI WO 2000062759 A1 20001026 (200101)* EN 40p A61K009-14 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000039574 A 20001102 (200107) A61K009-14 <--
ADT WO 2000062759 A1 WO 2000-DK184 20000413; AU 2000039574 A AU 2000-39574 20000413
FDT AU 2000039574 A Based on WO 200062759
PRAI **DK 1999-514 19990416**
IC ICM **A61K009-14**
AB WO 200062759 A UPAB: 20001230
NOVELTY - Solid pharmaceutical compositions for **parenteral injection** comprising a **binder** and at least one therapeutic agent consisting of at least one dosage, are new.
DETAILED DESCRIPTION - New pharmaceutical compositions for **parenteral injection** comprises a **binder** that constitutes at least 0.5 weight % of the composition. The composition comprises at least one **binding** agent that is a **carbohydrate** and optionally at least one non-crystallization agent, and forms an **amorphous** matrix.
INDEPENDENT CLAIMS are also included for the following:
(1) methods for preparing solid pharmaceutical compositions for **parenteral injection**; and
(2) devices containing the above-described solid pharmaceutical compositions adapted for **injection** through the epidermis or mucosa.
ACTIVITY - Analgesic; tranquilizer; antiarthritics; antibacterial; antidepressant; antidiabetics; antiemetic; hypotensive; antiinflammatory; antimigraine; antiparkinsonian; thrombolytic; antiviral; anorectic; cardiant; vasodilator; contraceptive; diuretic; hormonal; immunosuppressant; immunomodulator. No biological data is given.
MECHANISM OF ACTION - **Vaccine**; narcotic antagonist.
USE - The **parenteral injection** compositions are used to administer analgesics, anxiolytics, anti-arthritics, antibiotics, anticholinergics, antidepressants, antidiabetics, anti-emetics, antihistaminics, antihypertensives, anti-inflammatories, antimigraine agents, antiparkinsonism agents, antipasmodesics, antipsychotics, antithrombotics, antivirals, appetite suppressants, blood factors, cardiovascular drugs, cerebral vasodilators, chemotherapeutics, cholinergic agonists, contraceptives, coronary agents, diuretics, hormonal agents, immunosuppressants, growth factors, narcotic antagonists, opioids, peripheral vasodilators, tranquilizers, **vaccines**, immunogenic agents, immunizing agents, hormones, lipids, nucleic acids, nucleotides, oligonucleotides, **oligosaccharides**, organics, peptidomimetics, antibodies, peptides, **polysaccharides**, proteins, peptides, polypeptides, growth factors or blood factor, particularly insulin, glucagon, growth hormone, growth factors such as FVII or FVIII, GLP-1,

erythropoietin, thrombopoietin, interferon or their derivatives (claimed). They may be used for immunization (claimed).

ADVANTAGE - The compositions can be **injected** without the use of cannulae. They are long-term stable, solid and moldable. They have sufficient strength for **parenteral injection** but have a large content of therapeutic agent. They are particularly suitable for patients requiring frequent medication. They can be administered using epidermal or mucosal **injection** devices that provide easy, rapid and essentially painless **injection**. The avoidance of needles eliminates one source for cross-contamination in hospitals. They are stable long-term, even at ambient temperature and do not require special storage conditions. They are stable at ambient temperature in terms of compressive strength, the glassy nature of the **binder** and the geometry.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B04-B01B; B04-B03B; B04-B04D2; **B04-D01**; B04-E01; B04-G01; B04-H05; B04-H06; B04-H07; B04-H19; B04-J01; B04-J03A; B04-J03B; B04-J05; B04-N04; B11-B; B11-C04; B14-A01; B14-A02; B14-C01; B14-C03; B14-C09; B14-D01; B14-E05; B14-E12; B14-F01; B14-F02; B14-F02B; B14-F02D; B14-F02D1; B14-F04; B14-G02; B14-G03; B14-J01A3; B14-J01B3; B14-J01B4; B14-L01; B14-L06; B14-L09; B14-N08; B14-P01; B14-S04; B14-S11

TECH UPTX: 20001230

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred **Binder**: The **binder** constitutes 5 - 60 weight % of the composition. The **binder** essentially remains an **amorphous** matrix for at least 6 (12) months at ambient temperature. The **binder** can endure a pressure force of at least 10 (preferably at least 5) Newtons. The **binding** agent(s) comprise 50 - 97 weight % of the **binder**. The non-crystallization agent(s) comprise at least 1 weight % of the **binder**. The water content of the **binder** is less than 20 (preferably 1 - 5) weight %. The **carbohydrate** is a mono-, di- or **oligosaccharide**, the corresponding **sugar alcohol** or its derivative, preferably **maltose**, **sucrose**, **lactose**, **cellobiose**, **trehalose**, **maltulose**, **isomaltulose**, **maltitol**, **sorbitol**, **mannitol**, **glucose**, **fructose**, **raffinose**, **melezitose**, **dextran**, **mannose**, **sorbose**, **melibiose**, **sophrose**, **turanose**, **lactulose**, **stachyose**. The non-crystallization agent(s) are **carbohydrate**(s) different to the **binding** agent, preferably a mono-, di- or **oligosaccharide**, the corresponding **sugar alcohol** or its derivative, especially **maltose**, **sucrose**, **lactose**, **cellobiose**, **trehalose**, **maltulose**, **isomaltulose**, **maltitol**, **sorbitol**, **mannitol**, **glucose**, **fructose**, **raffinose**, **melezitose**, **dextran**, **mannose**, **sorbose**, **melibiose**, **sophrose**, **turanose**, **lactulose**, **stachyose**. The **binding** agent is **maltitol**, **sucrose**, **sorbitol** or **mannitol** and the non-crystallization agent is **sorbitol**, **maltitol** or **mannitol**. The **binding** agent is **maltitol** and the non-crystallization agent is **sorbitol** and/or **sugar alcohols** of maltotriose and higher **oligosaccharides**. The Tg (glass transition temperature) of the **binder** is at least 30 (preferably 40 - 120) degrees Centigrade. The **binder** does not reduce the stability of the therapeutic agent. The **binding** agent and non-crystallization agent are non-reducing **sugars**.

Preferred Compositions: At least 95 % of the strength of the composition is maintained after 6 (preferably 12) months at ambient temperature. The composition is essentially free from entrapped air. The compositions are **pellets** with a substantially cylindrical, triangular, square or

polygonal cross-section. The maximum cross-section of the **pellet** is less than 1 (preferably 0.7 - 0.3 or 0.6 - 0.4) mm. The compositions are in the shape of rods that are essentially cylindrical and pointed at one end. The top angle of the rod is 10 - 110 degrees (preferably 50 - 70 degrees). The length of the rod is less than 10 (preferably less than 2) mm. The volume of the composition is less than 5 (preferably less than 1) microliters. The composition can penetrate the epidermis of a human being with a force of less than 5 Newtons. The viscosity of the compositions is less than 50,000 (preferably 1,000 - 30,000) Pa in a sub-range temperature interval of 60 - 140 degrees Centigrade. The composition is **injection**-moldable in a sub-range temperature interval of 60 - 140 degrees Centigrade. At least 50 % of the therapeutic agent is released from the composition within 60 minutes after **injection**. The compositions further comprise additives including preservatives, adjuvants, stabilizers, lubricants or disintegrants. The composition is provided with a coating.
Preferred Therapeutic Agent - The therapeutic agent comprises at least 25 (preferably more than 40) weight % of the composition. The **binder** comprises at most 50 (preferably at most 40) weight % of the composition. The therapeutic agent is an analgesic, anxiolytic, anti-arthritic, antibiotic, anticholinergic, antidepressant, antidiabetic, anti-emetic, antihistaminic, antihypertensive, anti-inflammatory, antimigraine agent, antiparkinsonism agent, antipasmodesic, antipsychotic, antithrombotic, antiviral, appetite suppressant, blood factor, cardiovascular drug, cerebral vasodilator, chemotherapeutic, cholinergic agonist, contraceptive, coronary agent, diuretic, hormonal agent, immunosuppressant, growth factor, narcotic antagonist, opioid, peripheral vasodilator, tranquilizer, **vaccine**, immunogenic agent or immunizing agent, preferably a hormone, lipid, nucleic acid, nucleotide, oligonucleotide, **oligosaccharide**, organic, peptidomimetic, antibody, peptide, **polysaccharide** or protein, especially an (**amorphous** or crystalline) protein, peptide or polypeptide, most especially a hormone, antidiabetics, growth factor or blood factor, particularly a peptide chosen from insulin, glucagon, growth hormone, growth factor such as FVII or FVIII, GLP-1, erythropoietin, thrombopoietin, interferon or their derivatives.

L102 ANSWER 8 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-594247 [56] WPIX
DNC C2000-177449
TI Modifying carrier particle surface properties for pulmonary administration of **micronized** drugs from dry powder inhalers by producing fine fraction by mixing.
DC B05
IN BILZI, R; CHIESI, P; MUSA, R; VENTURA, P
PA (CHIE-N) CHIESI FARM SPA
CYC 90
PI WO 2000053158 A1 20000914 (200056)* EN 24p A61K009-14 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000034264 A 20000928 (200067) A61K009-14 <--
ADT WO 2000053158 A1 WO 2000-EP1773 20000302; AU 2000034264 A AU 2000-34264 20000302
FDT AU 2000034264 A Based on WO 200053158
PRAI IT 1999-MI455 19990305
IC ICM **A61K009-14**
ICS A61K009-72
AB WO 200053158 A UPAB: 20001106
NOVELTY - Modifying carrier particle surface properties for use in pulmonary administration of micronized drugs from dry powder inhalers comprises mixing treatment in a mixer with a rotating element, in order to produce a fine fraction of the carrier in situ.

USE - Dry powder pulmonary and/or nasal inhalation therapy can be used for a wide range of drugs, especially those use in treatment of respiratory diseases (e.g. anti-inflammatory steroids, e.g., beclomethasone dipropionate, flunisolide, budesonide, and their epimers; beta-agonists, e.g., salbutamol, salmeterol, formoterol, and terbutaline; and anticholinergics, e.g., ipratropium or oxytropium bromides).

ADVANTAGE - Dry powder inhalation is increasingly preferred to the liquid propellant method due to chlorofluorocarbon (CFC) environmental concerns, poor patient inhalation technique, and possibility of extensive oropharyngeal deposition. Dry powder inhalation generally is free from the first two disadvantages; there remain problems of deaggregation of the active ingredient from the carrier to deliver the drug, but this is made more efficient by the presence of a small proportion of fines only, obtained as indicated in a relatively mild mixing operation. In prior art, this was done by addition of fines as an extra operation. With too much fine content, as from the more vigorous operation of milling, flow properties and delivery may be adversely affected.

Dwg.0/1

FS CPI
FA AB; DCN
MC CPI: B01-B03; B10-B03B; B12-M01; B12-M11G; B14-K01
TECH UPTX: 20001106

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Process: The input carrier particles have a starting diameter of 90-150 microm, and the fine fraction produced has a mean aerodynamic diameter of less than 10 microm; the amount of this fraction with variation from the input diameter is less than 20%. The mixer is a stationary or rotating body mixer with a rotary element (i.e. blade or screw) or a high energy mixer (e.g. high shear) (especially a sigma blade mixer, with mixing rate 100-300 rpm). Powder mixing time is 5-360 (preferably 30) minutes. After mixing, optional additives, including lubricants (especially magnesium stearate, stearic acid, sodium stearyl fumarate or sodium benzoate), anti-adherents, and glidants, in total amount 0.05-2%, are added to the carrier, followed by one or more active ingredients, with a mean diameter less than 5 microm. Preferred Components: The carrier is a **saccharide**, preferably alpha-**lactose** monohydrate.

L102 ANSWER 9 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-534430 [49] WPIX
DNC C2000-159467
TI Stable solid dispersion composition comprises a low-solubility drug e.g. prazosin, nifedipine or trimazosin and at least one polymer e.g. cellulose acetate phthalate or cellulose acetate terephthalate.
DC A18 A96 B07
IN BABCOCK, W C; FRIESEN, D T; NIGHTINGALE, J A; SHANKER, R M; NIGHTINGALE, J A S
PA (PFIZ) PFIZER PROD INC
CYC 27
PI EP 1027886 A2 20000816 (200049)* EN 39p A61K009-14 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CA 2298214 A1 20000810 (200052) EN A61K045-00
JP 2000229887 A 20000822 (200055) 45p A61K047-38
ADT EP 1027886 A2 EP 2000-300815 20000202; CA 2298214 A1 CA 2000-2298214 20000209; JP 2000229887 A JP 2000-32955 20000210
PRAI US 1999-119401 19990210
IC ICM **A61K009-14**; A61K045-00; A61K047-38
ICS A61K009-10; A61K047-30
AB EP 1027886 A UPAB: 20001006

NOVELTY - A solid dispersion composition formed by solvent processing, comprising a low-solubility drug and at least one polymer (P1) having a glass transition temperature of at least 100 deg. C measured at 50% relative humidity, where a major portion of the drug once dispersed is **amorphous**, is new.

USE - The composition is used to prepare solid dispersions of drugs such as antihypertensives e.g. prazosin, nifedipine, trimazosin and

doxazosin, antianxiety agents, anticlotting agents, anticonvulsants, blood **glucose**-lowering agents, decongestants, antihistamines, antitussives, antineoplastics, beta blockers, antiinflammatories, antipsychotic agents, cognitive enhancers, cholesterol-reducing agents, antiobesity agents, autoimmune disorder agents, anti-impotence agents, antibacterial and antifungal agents, hypnotic agents, anti-Parkinsonism agents, anti-Alzheimer's disease agents, antibiotics, anti -depressants, and antiviral agents.

ADVANTAGE - The composition increases the bioavailability of the low-solubility drug by creating an enhanced concentration of the drug in an aqueous environment thus resulting in lower dosage of the drug. It has improved stability on storage due to the stabilizing effect of P1. Prior art solid dispersions show enhanced bioavailability of the low-solubility drug if administered shortly after preparation. Bioavailability decreases over time and the drug may revert to crystalline form on storage.

Dwg.0/3

FS CPI

FA AB; DCN

MC CPI: A03-A00A; A12-V01; B04-C02A2; B04-C02A3; B04-C02E3; B04-C03A; B04-C03B; B04-C03D; B06-D06; B07-D04C; B07-D04D; B14-A01; B14-A02; B14-A04; B14-C03; B14-E12; B14-F02B; B14-F04; B14-F06; B14-F07; B14-F09; B14-G02D; B14-H01; B14-J01A; B14-J01B; B14-J02D2; B14-K01B; B14-L09; B14-P02

TECH UPTX: 20001006

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Composition: The polymer (P1) and dispersion have a glass transition temperature of at least 105 (preferably 110) degrees C and at least 30 (preferably 50) degreesC measured at 50% relative humidity, respectively. The glass transition temperature of P1 at 0% relative humidity is 140 degreesC. The drug and P1 are soluble in a common non-aqueous solvent and the dispersion is formed by spray-drying. The composition further comprises a concentration-enhancing polymer (P2) which increases the maximum drug concentration (MDC) relative to a control composition comprising an equivalent quantity of undispersed drug. P1 and P2 are codispersed. The composition gives a maximum drug concentration at least 1.5 fold that of a control. The dispersion may be homogeneous. P1 absorbs less than 10 wt.% of water at 50% relative humidity. P1 has a glass transition temperature greater than that of P2.

TECHNOLOGY FOCUS - POLYMERS - Preferred Polymers: The polymer (P1) is cellulosic and has at least one ester- and/or an ether-linked aromatic substituent. The substituent is an ester- or ether-linked carboxylic acid-functional aromatic substituent. The ester-linked carboxylic acid-functional aromatic substituent is selected from structural isomers of phthalate, trimellitate and pyridine dicarboxylic acid and their alkyl substituted derivatives. The ether-linked carboxylic acid-functional aromatic substituent is selected from structural isomers of salicylic acid, ethoxybenzoic acid, propoxybenzoic acid, butoxybenzoic acid, ethoxyphthalic acid, propoxyphthalic acid, butoxyphthalic acid, ethoxynicotinic acid, propoxynicotinic acid, butoxynicotinic acid and alkyl-substituted derivatives. P1 has a degree of substitution of at least 0.2. P1 is selected from cellulose acetate phthalate, methyl cellulose acetate phthalate, ethyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate, hydroxypropyl methyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate succinate, cellulose propionate phthalate, hydroxypropyl cellulose butyrate phthalate, cellulose acetate trimellitate, methyl cellulose acetate trimellitate, ethyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate, hydroxypropyl methyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate succinate, cellulose propionate trimellitate, cellulose butyrate trimellitate, cellulose acetate terephthalate, cellulose acetate isophthalate, cellulose acetate pyridinedicarboxylate, salicylic acid cellulose acetate, hydroxypropyl salicylic acid cellulose acetate, ethylbenzoic acid cellulose acetate, hydroxypropyl ethylbenzoic acid cellulose acetate, ethyl phthalic acid cellulose acetate, ethyl nicotinic acid cellulose acetate, and ethyl picolinic acid cellulose acetate. The concentration-enhancing polymer (P2)

is selected from hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose acetate phthalate, hydroxypropyl methyl cellulose acetate, hydroxypropyl methyl cellulose succinate, hydroxypropyl methyl cellulose phthalate, hydroxypropylmethyl cellulose, hydroxypropylcellulose, methyl cellulose, hydroxyethyl cellulose, hydroxy ethyl methyl cellulose, hydroxy ethyl cellulose acetate, hydroxyethyl ethyl cellulose, hydroxy ethyl methyl cellulose acetate succinate, hydroxyethyl methyl cellulose acetate phthalate, carboxymethyl cellulose, carboxyethyl cellulose, polyvinyl alcohol, polyvinyl alcohol polyvinyl acetate copolymers, polyethylene glycol, polyethylene glycol polypropylene glycol copolymers, polyvinyl pyrrolidone, polyethylene polyvinyl alcohol copolymers, carboxylic acid-functionalized polymethacrylates, amine-functionalized polymethacrylates, chitosan, and chitin.

L102 ANSWER 10 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-514764 [46] WPIX
DNC C2000-153565
TI Preparing particles for agglomeration, useful e.g. as pharmaceutical carriers for delivery by oral inhalation, by two stages of micronization with intermediate curing step.
DC B01 B05
IN ECKHART, C G; MITCHELL, M B; YANG, T; YU, S K C
PA (SCHE) SCHERING CORP
CYC 87
PI WO 2000044352 A1 20000803 (200046)* EN 29p A61K009-14 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CZ DE DK DM EE ES FI GB GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT LU LV MA MD MG MK MN MX NO NZ PL PT RO RU SE SG SI SK SL TJ TM TR TT TZ UA UZ VN YU ZA
AU 2000034700 A 20000818 (200057) A61K009-14 <--
ADT WO 2000044352 A1 WO 2000-US496 20000127; AU 2000034700 A AU 2000-34700 20000127
FDT AU 2000034700 A Based on WO 200044352
PRAI US 1999-239486 19990128
IC ICM **A61K009-14**
ICS A61K009-72
AB WO 200044352 A UPAB: 20000921
NOVELTY - Production of a particulate substance (A) comprises micronizing a particulate material of first particle size distribution (PSD) to intermediate particles (IP) having a different PSD and increased **amorphous** content (AC), curing IP to reduce the AC and remicronizing the cured IP to produce particles of third PSD and having AC higher than that of cured IP.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) (A) produced by the above method; and

(2) particle mixture (B) comprising particulate solid carrier (C) with PSD such that at least 70 vol% of particles are not over 5 micron and a pharmaceutically active agent (I) of PSD such that at least 80 vol% are not over 5 micron, and with total convertible AC for the mixture corresponding to a heat of crystallization (HC) 2-16 J/g.

USE - The method is used to produce agglomerates containing pharmaceuticals (I) and/or solid carriers, for preparation of tablets or capsules, or for direct administration by oral inhalation.

ADVANTAGE - The intermediate curing step eliminates (or at least reduces) the convertible AC present in the initial micronized product. Once this product has been (partially) recrystallized, the degree of AC in the final product will be within acceptable limits, i.e. this product will not be too strong or hard and/or will not deliver an unacceptable fine fraction from a powder inhaler.

Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B01-C02; B04-H05; B04-J03A; B10-B03; B12-M01B; B12-M11E

TECH UPTX: 20000921
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Materials: The remicronized particles are of a solid carrier and have PSD of at least 60, preferably 80 vol% less than 5 micron and predetermined convertible AC corresponding to HC of 1-20, preferably 2-16 and especially 3.8-7, Joules/g. The particulate material comprises **lactose** or pharmaceutically active material e.g. mometasone furoate, eformoterol (both claimed) but many others are disclosed, e.g. dexamethasone, triamcinolone, salbutamol, sodium cromoglycate, insulin, interferons..
Suitable carriers are polyhydroxy aldehydes or ketones (specifically sugars) or amino acids. (A) may also include a (I) which has at least 80, preferably 90 vol% of particles not over 5 micron and convertible AC content corresponding to HC 1-20 J/g. A particularly preferred composition comprises mometasone furoate and has HC 3.2-6 J/g.
Preferred Process: The curing step preferably comprises exposing IP to relative humidity of 35-45% at 20-25degreesC, for at least 4 hour, when the material is spread as a layer or cake about 5 cm thick. More than two micronization steps may be used, provided each one (except the last) is followed by a curing step.

L102 ANSWER 11 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-500307 [45] WPIX
DNC C2000-150306
TI Controlled release dosage form for e.g. antiinflammatory drug comprises has water permeable coating controlling influx of water to core comprising osmotic agent and low solubility drug.
DC A96 B05 B07
IN APPEL, L E; CURATOLO, W J; HERBIG, S M; NIGHTINGALE, J A; THOMBRE, A G; NIGHTINGALE, J A S
PA (PFIZ) PFIZER PROD INC
CYC 27
PI EP 1027888 A2 20000816 (200045)* EN 29p A61K009-26
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2000229846 A 20000822 (200045) 24p A61K009-22
CA 2298238 A1 20000810 (200052) EN A61K009-14 <--
ADT EP 1027888 A2 EP 2000-300572 20000126; JP 2000229846 A JP 2000-33132 20000210; CA 2298238 A1 CA 2000-2298238 20000209
PRAI US 1999-119406 19990210
IC ICM **A61K009-14**; A61K009-22;. A61K009-26
ICS A61K009-52; A61K031-135; A61K031-137; A61K031-17; A61K031-36; A61K031-40; A61K031-404; A61K031-44; A61K031-4422; A61K031-497; A61K031-505; A61K031-517; A61K031-522; A61K045-00; A61K047-32; A61K047-34; A61K047-38; A61P009-12; A61P013-00; A61P025-18; A61P029-00
AB EP 1027888 A UPAB: 20000918
NOVELTY - Controlled release dosage form comprises:
(1) a core comprising an osmotic agent and low solubility drug in a solid dispersion in a polymer and
(2) a water permeable coating.
The coating controls influx of water to the core from an aqueous environment to extrude at least part of the core through at least one delivery port to the aqueous environment.
DETAILED DESCRIPTION - Controlled release dosage form comprises:
(1) a core comprising an osmotic agent and a low solubility drug in a solid dispersion in a polymer and
(2) a water permeable coating around the core having at least one delivery port.
The coating controls influx of water to the core from an aqueous environment to extrude at least part of the core through at least one delivery port to the aqueous environment. The coating is non dissolving and non eroding during release of the drug. At least a major part of the drug is **amorphous**.
USE - Used for treating diseases and disorders.
ADVANTAGE - The controlled release dosage form delivers a low solubility drug with a short elimination half-life which improves drug

bioavailability.
Dwg.0/7
FS CPI
FA AB; DCN
MC CPI: A12-V01; B04-C02; B04-C03; B06-D01; B07-H; B10-A13D; B12-M10A; B14-A01; B14-A02; B14-A03; B14-A04; B14-C03; B14-D01; B14-D01A; B14-D03; B14-D07A; B14-E08; B14-E10; B14-E11; B14-E12; B14-F01; B14-F02B; B14-F04; B14-F06; B14-F07; B14-F09; B14-G02D; B14-H01; B14-J01; B14-K01B; B14-K01E; B14-L09; B14-N08
TECH UPTX: 20000918

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred drug: The drug is **amorphous**. The drug comprises an antihypertensive, anxiolytic, anticlotting agent, blood **glucose** lowering agent, antihistamine, antitussive, antiinflammatory, antiarteriosclerotic agent, antipsychotic agent, cognitive enhancer, cholesterol reducing agent, antiobesity agent, autoimmune disorders agent, hypnotic agent, anti-Parkinsonism agent, antibiotic, antiviral agent, antiimpotence agent, antineoplastic, sedative, barbiturate, nutritional agent, beta-blocker, emetic, antiemetic, diuretic, anticoagulant, cardiotonic, androgen, corticoid, anabolic agent, antidepression agent, antiinfective agent, coronary vasodilator, carbonic anhydrase inhibitor, antifungal, antiprotozoal, gastrointestinal agent, dopaminergic agent, anti-Alzheimer's disease agent, antiulcer agent, platelet inhibitor or glycogen phosphorylase inhibitor.
The antihypertensive comprises prazosin, nifedipine, trimazosin or doxazosin. The antipsychotic agent comprises ziprasidone. The blood **glucose** lowering agent comprises glipizide. The antiimpotence drug comprises sildenafil. The antiinflammatory agent comprises(+)-N-(4-(3-(4-fluorophenoxy)phenoxy)-2-cyclopenten-1-yl)-N-hydroxyurea. The antidepression agent comprises fluotexine, paroxetine, venlafaxine, sertraline, (3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridin-4-yl)-(1-ethylpropyl)-amine or 3,5-dimethyl-4-(3'-pentoxy)-2-(2',4',6'-trimethylphenoxy)-pyridine. The glycogen phosphorylase inhibitor comprises (R-(RasteriskSasterisk))-5-chloro-N-(2-hydroxy-3-(methoxymethylamino)-3-oxo-1-(phenylmethyl)propyl)propyl)-1H-indole-2-carboxamide or 5-chloro-1H-indole-2-carboxylic acid (1S)-benzyl-3-((3R,4S)-dihydroxypyrrolidin-1-yl)-(2R)-hydroxy-3-oxypropyl)amide.
Preferred dosage form: The delivery port comprises pores in the coating or is formed by laser drilling, erosion of a plug of water soluble material or by rupture of a relatively small part of the coating. The osmotic agent comprises a solute and water swellable polymer. The osmotic agent is in a first layer and the solid dispersion is in a second layer.
The dosage form also comprises a solubility enhancing agent comprising e.g. organic acids or their metal salts, glycerides, polyethylene glycol esters, sorbitan esters or carbonate salts.
The dosage form provides a maximum concentration of the drug in a use environment that is at least 1.2 times that of a control dosage form comprising an identical dosage form containing an equivalent amount of undispersed drug and an area under the curve (AUC) in a use environment that is at least 12.25 times that of a control dosage form comprising an identical form containing an equivalent amount of undispersed drug. The dosage form provides a maximum drug concentration in the blood at a tmax which is at least 30 minutes longer but not more than 24 hours longer than the tmax observed for the control dosage form.
The environment of use is the gastrointestinal tract.

TECHNOLOGY FOCUS - POLYMERS - The coating is formed from e.g. polyacrylic acids and esters, polymethacrylic acids and esters, copolymers of polyacrylic and polymethacrylic acids and esters, cellulose esters, cellulose ethers or cellulose ester/ethers, polyethylene glycol, starch, **dextran**, polyethersulfones, polystyrenes, polyvinyl halides or waxes.
The water swellable hydrophilic polymer comprises e.g. hydrophilic vinyl and acrylic polymers, **polysaccharide** alginates, polyethylene oxide, polyvinyl alcohol, carrageenan, gelatin, xanthan gum or sodium starch glycolate.

The dispersion polymer comprises ionizable cellulosic polymers, non-ionizable cellulosic polymers and vinyl polymers and copolymers having OH, alkylacyloxy or cyclic amido substituents.

L102 ANSWER 12 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-491010 [43] WPIX
DNN N2000-364396 DNC C2000-147555
TI Composition for delivering polyionic pharmaceuticals, especially nucleic acids, useful e.g. in preventing restenosis, has active agent in condensed form on exterior of a **matrix**.
DC A96 B07 D16 D22 P32
IN LEVY, R J
PA (CHIL-N) CHILDRENS HOSPITAL PHILADELPHIA
CYC 90
PI WO 2000041647 A1 20000720 (200043)* EN 73p A61F002-02
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000028537 A 20000801 (200054) A61F002-02
ADT WO 2000041647 A1 WO 2000-US1317 20000119; AU 2000028537 A AU 2000-28537 20000119
FDT AU 2000028537 A Based on WO 200041647
PRAI US 1999-234011 19990119
IC ICM A61F002-02
ICS A61F002-06; A61F013-00; A61K009-127; **A61K009-14**; A61K009-16; A61K047-00; A61K047-48
AB WO 200041647 A UPAB: 20000907
NOVELTY - Composition (A) for delivering a polyionic bioactive agent (I) comprising a matrix and where most of the (I) present on the exterior portion of the matrix is in a condensed form.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(a) a surface coated with (A);

(b) an implantable device with a surface coated with (A);

(c) preparation of (A) comprising suspending (I), in non-condensed form, in a biodegradable matrix, and then treating the exterior part of the matrix with an agent (II) that condenses (I);

(d) preparation of (A) comprising contacting a matrix with (I) on the outside with (II);

(e) delivery of (I) to an animal by implanting (A);

(f) kits for preparing (A) comprising a matrix or a composition comprising a matrix and (I) on its exterior, where most of the (I) present on the exterior portion of the matrix is in a condensed form

(g) kits for coating an implantable device with (A) comprising a polymeric matrix suspended in a solvent and a condensing agent as in (II) with a charge opposite to that of (I), or comprising a suspension of biocompatible polymeric matrix monomers, a polymerization indicator, and a (II) with a charge opposite to that of (I); and

(h) storing nucleic acid (Ia) comprising suspending it in a matrix and contacting the matrix with a polycationic condensing agent.

ACTIVITY - Vulnerary; vasotropic; cytostatic.

MECHANISM OF ACTION - Gene therapy.

USE - (A) are used, in human or veterinary medicine, for the sustained delivery of (I), especially nucleic acids (but also e.g. DNA-binding proteins and transcription factors) to tissues. The compositions are especially useful for delivering wound-healing proteins, anti-restenotic proteins or antisense oligonucleotides and oncogenes or anti-oncogene antisense molecules, (e.g. for treatment of brain tumors). (A) can also be used for the long term storage of a nucleic acid.

ADVANTAGE - In condensed form, (I) is more stable, provides sustained release and often is better able to cross cell membranes.

Dwg.0/1
FS CPI GMPI

FA AB; DCN
MC CPI: A12-V01; B04-E02; B04-E03; B04-E06; B04-E08; B04-H01; B04-H06; B04-J01; B04-N02; B11-C04A; B11-C06; B12-M05; B12-M10A; B14-F02D; B14-H01B; B14-N17B; B14-S03; D05-H12A; D05-H12B; D05-H12D2; D05-H12D4; D05-H12E; D09-C01
TECH UPTX: 20000907
TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Composition: Preferably all (I) at the exterior of the matrix is condensed and all (I) may be present at the exterior. The matrix may have several exterior parts and optionally at least 1 interior part that includes suspended (I), mostly in non-condensed form.
Preferred Matrix: The matrix is made from a charged biocompatible (optionally biodegradable) material or polymer, e.g. an alginate, agarose, **dextran**, dextrin, metal or alloy, hydroxyapatite, tricalcium phosphate, cocoa butter, wax or a ceramic. A preferred polymer is poly(lactate-co-glycolate), PLGA.
Preferred Device: Implantable devices are preferably wound dressings, sutures, particles, vascular stents or bulk materials. Vascular stents are made of PLGA with an exterior coating of polylysine and containing an anti-restenotic nucleic acid. Sutures are coated with many (at least 20) layers of PLGA and (I) is preferably a nucleic acid expressing a wound-healing protein. The particles have a diameter of at most 900 (preferably 1) micro m and bulk materials contain a (I) that is an expression vector encoding an oncogene or antisense oligonucleotide directed against an oncogene.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Condensing Agent: (II) is a polyionic agent with a charge opposite to that on (I), preferably a polycationic agent e.g. polyarginine, polyhistidine, myelin basic protein, magnesium or calcium ions, spermine, polyethyleneimine and especially poly-L-lysine. Alternatively (II) is a polyanionic agent, preferably a nucleic acid.
Preferred Bioactive Agents: The bioactive agents are preferably nucleic acids (or their analogs), plamids, antisense oligonucleotides, vectors, ribozymes, viral genomes or gene fragments etc. Most preferred are (i) an expression vcetor producing a wound-healing or anti-restenotic protein or (ii) an anti-restenotic antisense sequence. Specific wound-healing proteins are, e.g. transforming growth factor-beta (TGFbeta), fibroblast growth factor, platelet-derived growth factor and growth hormones. Anti-restenotic proteins are e.g. TGFbeta, Rb, p21 and anti-restenotic oligonucleotides are derived from c-myb, c-myc or PCNA. Alternatively, (I) is polycationic, e.g. a DNA-binding protein, histone, cationic polymer, cadaverin, putrescine, spermine or spermidine.
Preferred Oncogenes: The oncogene is preferably 1 of about 80 given in the specification, e.g. abl, bcl2alpha, brcal or 2, jun, myb and nras.

TECHNOLOGY FOCUS - POLYMERS - Preferred Polymers: Typical of many polymers for use as a matrix are, e.g. polycaprolactone, polyacrylate, polyacrylonitrile, polyurethane, poly(alkylene oxide), silicone rubber and especially PLGA. A suitable cationic (II) is polyethyleneimine.

L102 ANSWER 13 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-411804 [35] WPIX
DNC C2000-124740
TI Converting **amorphous** and/or meta-stable crystalline preformed particles into crystalline state for use in pharmaceuticals especially for oral or nasal administration.
DC B05
IN BISRAT, M; DEMIRBUEKER, M; MOSHASHEE, S; NYQVIST, H
PA (ASTR) ASTRAZENECA AB
CYC 90
PI WO 2000030614 A1 20000602 (200035)* EN 27p A61K009-14 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS

LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL
TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000020104 A 20000613 (200043) A61K009-14 <--
ADT WO 2000030614 A1 WO 1999-SE2154 19991122; AU 2000020104 A AU 2000-20104 19991122
FDT AU 2000020104 A Based on WO 200030614
PRAI SE 1998-4000 19981123
IC ICM **A61K009-14**
ICS A61K031-00; A61K038-00
AB WO 200030614 A UPAB: 20000725
NOVELTY - Converting **amorphous** and/or meta-stable crystalline regions of preformed particles into a crystalline state comprises placing the particles in an apparatus, treating with supercritical or subcritical fluid comprising an anti-solvent and a solvent and recovering the particles.
DETAILED DESCRIPTION - Converting **amorphous** and/or meta-stable crystalline regions of preformed particles into a crystalline state comprises:
(a) placing the particles in an apparatus;
(b) treating with supercritical or subcritical fluid comprising an anti-solvent and a solvent; and
(c) recovering the particles.
INDEPENDENT CLAIMS are also included for:
(i) a pharmaceutical formulation comprising an active substance and one or more excipients including at least one produced as above; and
(ii) particles of crystalline state having been converted from particles with **amorphous** and/or meta-stable crystalline regions and having a thermal activity monitor (TAM) value of less than 3 (preferably less than 0.5) J/g when recovered from the process.
USE - For converting **amorphous** and/or meta-stable crystalline regions of preformed particles into a crystalline state to give particles suitable for use in pharmaceutical formulations, especially for oral or nasal administration of medicaments for treating allergic and/or inflammatory conditions of the nose or lungs, chronic obstructive pulmonary disease, rhinitis, asthma, inflammatory bowel disease, Crohn's disease or ulcerative colitis.
ADVANTAGE - Crystalline particles are more stable than **amorphous** and/or meta-stable crystalline particles.
Dwg.0/1
FS CPI
FA AB; DCN
MC CPI: B04-A06; B04-C02; **B04-D01**; B04-J02; B04-N04; B07-A02B; B07-D04C; B07-D05; B07-E01; B10-B01A; B10-B03B; B12-M11H; B14-C03; B14-E08; B14-E10C; B14-G02A; B14-J02C1; B14-K01; B14-N04
TECH UPTX: 20000725
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Process: Particles (preferably pharmaceutically acceptable mono-, di-, tri-, oligo- or poly-**saccharides** or **polyols** or their esters, acetals, salts or solvates, especially **lactose** monohydrate, with a mass median diameter of less than 100 (preferably less than 10) mum) are treated at 5-50 (preferably 15-30) degrees C above the critical temperature of the anti-solvent (preferably carbon dioxide) and at 10-300 (preferably 30-100) bar higher than the critical pressure. Supercritical or subcritical fluid is saturated with solvent (preferably a polar solvent, especially water) at 15-50 (preferably 25-40) % of total solvent-saturation. After step (b) the particles are treated with a dry anti-solvent and after step (c) the particles have a TAM of less than 3 (preferably less than 0.5) J/g and a reduction factor compared to before step (a) of more than 5 (preferably more than 100).
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Formulation: The active agent is a glucocorticosteroid, anticholinergic, leukotriene antagonist, protein, peptide and/or beta-agonist (preferably formoterol, salbutamol, rimiterol, fenoterol, reproterol, pirbuterol, bitolterol, salmeterol, clenbuterol, procaterol, broxaterol, picumeterol, mabuterol, terbutaline, isoprenaline, orciprenaline and/or adrenaline and/or their esters, acetals, salts or solvates).

L102 ANSWER 14 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-376271 [32] WPIX
DNC C2000-113706
TI Composition useful for delivery of genes, especially DNA into the cells, for the purpose of altering the function, gene expression or viability of cells, comprises stabilized nucleic acid-polycation condensates.
DC A96 B04 D16
IN CHEN, X; D'ANDREA, M J; MA, C
PA (SELE-N) SELECTIVE GENETICS INC
CYC 89
PI WO 2000027361 A1 20000518 (200032)* EN 78p A61K009-14 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000016055 A 20000529 (200041) A61K009-14 <--
US 6251599 B1 20010626 (200138) C12Q001-68
ADT WO 2000027361 A1 WO 1999-US25884 19991103; AU 2000016055 A AU 2000-16055 19991103; US 6251599 B1 US 1998-187727 19981106
FDT AU 2000016055 A Based on WO 200027361
PRAI US 1998-187727 19981106
IC ICM **A61K009-14**; C12Q001-68
ICS A61K009-10; A61K009-19; A61K047-26; A61K047-36; A61K047-42; A61K048-00
AB WO 200027361 A UPAB: 20000706
NOVELTY - A composition (I) comprising a nucleic acid molecule (II) condensed with a polycation (III) in a liquid medium, forming a particle which increases in size by less than one-fold during storage in the liquid medium for one week at about 2-8 deg. C.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a condensate (C) comprising a (II), (III) and at least one excipient from zwitterion, an **amorphous** cryoprotectant, crystalline bulking agent, and their mixtures;
(2) a lyophile, prepared by combining water, (II), (III) and an excipient forming particles, and removing the water from the mixture;
(3) a composition comprising (II), (III), an excipient, and a ligand covalently attached to at least one of the components, the composition comprises a particle which increases in size by less than one-fold during liquid storage for one week at 2-8 deg. C;
(4) a method of preparing a condensed nucleic acid comprising admixing (II) and (III) in a liquid medium, incubating the mixture under conditions in which (II) and (III) condense to form particles, lyophilizing the mixture to remove the liquid medium, producing a lyophile comprising particle, and reconstructing the lyophile with a predetermined volume of a reconstituting medium to form a reconstituted composition comprising particle which increase in size by less than one-fold during liquid storage for one week at 2-8 deg. C; and
(5) a composition for the delivery of (II) to a mammalian cell, prepared by the method of (4).
USE - (I) is useful for a variety of applications including delivery of exogenous (II), especially DNA into the cells, for the purpose of altering the function, gene expression or viability of cells.
ADVANTAGE - Unlike prior art compositions, (I) has the capability of maintaining their stability under a variety of different conditions.
Dwg.0/9
FS CPI
FA AB; DCN
MC CPI: A10-E01; A12-V01; B04-C01; B04-C02C; B04-C03; B04-E01; B04-E08; B04-N04; B10-A07; B10-B02; B14-S03; D05-H10; D05-H12E; D05-H18
TECH UPTX: 20000706
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Composition: (I), (C) and lyophile further comprise an excipient, which is a zwitterion, an

amorphous cryoprotectant, a crystalline bulking agent, or their mixtures. The zwitterion is an amino acid, polypeptide or a biological buffer, and preferably comprises glycine or a polypeptide comprising a glycine residue. The amino acid has a pKa of 3-9. The cryoprotectant is a **saccharide**, **polyol** or a protein. (III) is a polyamino acid, preferably with one or more cationic and/or basic amino acids, especially poly-L-lysine, poly-D-lysine or poly-DL-lysine, or protamine, histone or a polymer. The bulking agent is D-**mannitol**, **trehalose** or **dextran**. (II) is a genome or plasmid DNA comprising a therapeutic or diagnostic gene having a concentration less than 20-40mg/ml. The ratio of (II):(III) charge ratio ranges between 1:1-1:2. (I) further comprises a ligand preferably a polypeptide reactive with a cell growth factor receptor, attached to a (III) forming a polycation-ligand conjugate. The ratio of polycation-ligand conjugate to the (II) is less than 5:1 (w:w). The ligand is a peptide reactive with a cell growth factor, preferably a fibroblast growth factor (FGF) receptor.
Preferred Condensate: The condensate comprises a mixture of first zwitterion and second zwitterion. The excipient comprises a zwitterion, an **amorphous** cryoprotectant and a crystalline bulking agent.
Preferred method: The liquid storage step is for one week at 20-28degreesC.
Preparation: (I) is prepared by mixing (II) and (III) in a liquid medium, and incubating the mixture under condensation conditions to form particles (p1) with a hydrodynamic diameter in the range of 80-100nm. The mixture is lyophilized to remove the liquid medium, producing a lyophile comprising particles, and the lyophile is reconstituted with a predetermined volume of a reconstituting medium to form particles (p2) with a hydrodynamic diameter of less than 200nm, preferably less than 100nm, especially less than 80nm, that increase in size less than one-fold during storage reconstituting liquid for one week at 2-8degreesC. The average size of (p2) is less than twice the average particle size of (p1), and the concentration of (p2) is greater than the concentration of (p1). The method further comprises an additional step of mixing an excipient into the medium before lyophilizing. The concentration of (II) in the mixture of (II) and (III), is less than 0.5mg/ml and the concentration of (II) in the reconstituted composition is less than 20mg/ml.

L102 ANSWER 15 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-302771 [26] WPIX
CR 1999-152712 [13]
DNC C2000-091667
TI Flowable compositions for making comestible units, especially chewable tables, comprising partially crystallized shearform particles treated with ethanol or **lactose** and particles containing at least one bioactive agent..
DC B07 D21
IN CURRINGTON, J W; KAMATH, S V; MISRA, T K; MONTWILL, B; RAIDEN, M; SANGHVI, P P; SISAK, J R
PA (FUIS-N) FUISZ TECHNOLOGIES LTD
CYC 1
PI US 6048541 A 20000411 (200026)* 11p A61K006-00
ADT US 6048541 A CIP of US 1997-915067 19970820, US 1998-132986 19980812
FDT US 6048541 A CIP of US 5869098
PRAI US 1998-132986 19980812; US 1997-915067 19970820
IC ICM A61K006-00
ICS A61K007-00; **A61K009-14**; A61K009-20
AB US 6048541 A UPAB: 20000624
NOVELTY - A flowable composition for making comestible units comprising:
(a) partially crystallized shearform particles treated with at least one of ethanol and **lactose**; and
(b) particles containing at least one bio-affecting agent.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the preparation of fast dissolving comestible units comprising;
(a) providing **amorphous** shearform particles;
(b) treating the particles with at least one material selected from ethanol or **lactose**;

(c) blending optionally coated particles containing at least one bio-affecting agent with the treated shearform particles; and

(d) shaping and compressing the blend to produce comestible units.

USE - The flowable composition is used for making comestible units, especially preferred units are fast-dissolving, chewable tablets.

ADVANTAGE - The compositions have enhanced cohesive and self-binding properties and so tableting can take place without the addition of glycerine, to give tablets which disintegrate rapidly when placed in the mouth, especially when chewed.

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: **B04-D01**; B10-E04D; B12-M11B; B12-M11H; D08-B
TECH UPTX: 20000531

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Processes: The shearform particles are preferably pretreated with **lactose**. The particles containing the bio-affecting agent can be selected from a wide range of active agents however the claimed active agents are selected from analgesics, antacids and vitamins and are in the form of microspheres. The particles may optionally be coated.

L102 ANSWER 16 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-294139 [26] WPIX
DNC C2000-089034
TI **Parenteral** drug administration composition with depot and controlled release comprises active agent and water soluble **polysaccharide** microparticles as carrier.
DC B07
IN BENGS, H; BOEHM, G; GRANDE, J; SCHUTH, S
PA (AVET) AVENTIS RES & TECHNOLOGIES GMBH & CO KG
CYC 29
PI DE 19847593 A1 20000420 (200026)* 10p A61K009-14 <--
WO 2000021505 A2 20000420 (200027) DE A61K009-16
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA CN CZ JP KR NO NZ PL US ZA
AU 9961989 A 20000501 (200036) A61K009-16
ADT DE 19847593 A1 DE 1998-19847593 19981015; WO 2000021505 A2 WO 1999-EP7300 19991002; AU 9961989 A AU 1999-61989 19991002
FDT AU 9961989 A Based on WO 200021505
PRAI DE 1998-19847593 19981015
IC ICM **A61K009-14**; A61K009-16
AB DE 19847593 A UPAB: 20000531

NOVELTY - A composition for **parenteral** administration comprises active agents (A) and a carrier material (B) consisting of spherical microparticles of average diameter 1 nm to 100 micro m, at least partly of water-insoluble linear **polysaccharide** (PS).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a suspension comprising the above composition plus a suspension medium (specifically sterile saline).

USE - The compositions are useful (optionally in suspended form) in human or veterinary medicine for the administration of drugs (A) by **injection** (claimed). Typical (A) are the LHRH analog buserelin (for treating prostate cancer or endometriosis), erythropoietin (for stimulating erythrocyte growth), analgesics, antiallergic agents, growth hormones, steroids (for hormone treatment or contraception), bis-phosphonates, calcitonin (for treating osteoporosis), psychiatric drugs or any proteins or peptides which are decomposed in the gastrointestinal tract. The use of the microparticles is also claimed for **parenteral** application and as contrast agent; e.g. the particles (B) may be administered without an active agent as contrast agents for ultrasonic diagnosis.

ADVANTAGE - The compositions have depot and controlled release effects (claimed), providing controlled release over a long period and targeted drug biodistribution, bioavailability and resorption. The carriers and their biodegradation products have good biocompatibility, and the carrier particles form stable suspensions without the need for

additives. The compositions readily pass through cannulas (even of low diameter) or small diameter **injection** needles.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-C01B; B04-C02; B04-J02; B04-N06; B11-C08; B12-K04C1; B12-M10A; B14-C01; B14-D01; B14-D01C; B14-G02A; B14-H01; B14-J01; B14-N01; B14-N14; B14-P01
TECH UPTX: 20000531
TECHNOLOGY FOCUS - POLYMERS - Preferred **Polysaccharides**: PS is biotechnically obtained, and is preferably a linear polyglucan, specifically a poly-(1,4-alpha-D-glucan) or a poly-(1,3-beta-D-glucan). It may be chemically modified, specifically esterified and/or etherified in at least one or the 2-, 3- and 6-positions.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The depth of irregularities on the surface of the particles is at most 20% (preferably at most 10%) of the maximum particle diameter. The microparticles have a dispersity D of 1.0-10.0. (A) is mixed with (B), encapsulated in (B) or absorbed on the surface of (B).

L102 ANSWER 17 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-284193 [25] WPIX
DNC C2000-085898
TI Association of active agent with colloidal polymer, preferably new polymeric branched **polyol** ester, useful for controlled transmucosal administration of e.g. peptide, DNA construct or vaccine.
DC A96 B04 B07 D16
IN BREITENBACH, A; JUNG, T; KAMM, W; KISSEL, T
PA (BREI-I) BREITENBACH A; (JUNG-I) JUNG T; (KAMM-I) KAMM W; (KISS-I) KISSEL T
CYC 1
PI DE 19839515 A1 20000309 (200025)* 39p A61K009-14 <--
ADT DE 19839515 A1 DE 1998-19839515 19980829
PRAI DE 1998-19839515 19980829
IC ICM **A61K009-14**
AB DE 19839515 A UPAB: 20000524
NOVELTY - A pharmaceutical composition contains at least one colloidal polymer-active agent association (A).
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for novel polymers (I) which are branched **polyol** esters consisting of a central molecule (II) to which short-chain, biodegradable hydroxycarboxylic acid ester groups (III) are attached. The reaction parameters (i.e. natural and amount of (II) and catalyst system, nature and length of (III), reaction temperature and reaction time) are selected to optimize (I) for use as the polymer component of (A).
ACTIVITY - Cytostatic; antiinflammatory; antibiotic; vaccine.
MECHANISM OF ACTION - None given.
USE - (A) are used for mucosal adminstration of the active agent, which is specifically an active peptide, protein, enzyme, enzyme inhibitor, antigen, cytostatic agent, antiinflammatory, antibiotic, DNA construct or growth factor (all claimed). Use as a vaccine is also claimed. (I) is used as the polymer component of (A) (claimed).
ADVANTAGE - Administration in the form of (A) improves the stability, bioavailability, biodistribution, activity and/or resorption of the active agent, and may reduce side-effects. (A) can be prepared under mild conditions which cause no degradation of unstable active agents. The polymers can be associated with most macromolecular active agents without causing degradation; can provide controlled and targeted release; can be prepared in a small number of steps; are biocompatible, biodegradable and non-toxic to surrounding tissue; have long dwell time on mucosal surfaces to cause enrichment of active agents at mucosal surfaces; may increase cellular uptake; and may induce an immune response when use with an immunizing antigen or DNA construct.
Dwg.0/22
FS CPI

FA AB; DCN
MC CPI: A05-E02; A09-A07; A12-V01; B04-C01; B04-C02; B04-C03; B04-E01; B04-L01; B04-N04; B12-M10; B14-A01; B14-C03; B14-H01B; B14-S11B; B14-S11C; D05-A02; D05-H07; D05-H10; D05-H12
TECH UPTX: 20000524
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The association is a polymer-active agent complex, typically formed spontaneously in situ by combining an aqueous solution containing the polymer with a component containing the active agent (optionally in chemically bonded or physically associated form). Alternatively the polymeric carrier is converted into colloidal form by controlled precipitation, in which case the active agent is adsorbed on the polymer colloid (formed previously or in situ), enclosed in the polymer matrix in situ during particle formation or bonded covalently to at least one functional group on the polymer or the particle surface. The colloidal particle size is less than 1 mm, especially 10-10000 nm.
TECHNOLOGY FOCUS - POLYMERS - Preferred Central Molecules: (II) are optionally modified **polyols**, specifically: (i) linear synthetic polymers containing 7-500 OH groups, especially polyvinyl alcohol having a polymerization degree of 7-500 and a saponification degree of 70-89% or a copolymer of vinyl alcohol with vinyl acetate, -pyrrolidone, -amine, -imidazole, -pyridine, -sulfonic acid or -phosphoric acid; or (ii) linear, branched or cyclic, charged or uncharged **polysaccharides**, preferably starch (or its components), glycogen, cellulose (or its components), **dextran**, tunicin, inulin, chitin, alginate, pectin, mannan, galactan, xylan, other polyoses, chondroitin sulfate, heparin, hyaluronic acid, other glycosaminoglycans, murein, dextrin, cyclodextrin, chitosan or their partially hydrophobicized derivatives (preferably methyl or ethyl ethers, esters or urethanes). (II) optionally contain carboxy, sulfobutyl, sulfopropyl, butylamine, propylamine and/or ethylamine groups.
Preferred Side-Chains: (III) are derived from D- or L-lactic and/or glycolic acid or from D-, L- or D,L-lactide and/or glycolide.
Preferred Polymers: (I) may prepared using (II) in the form of a halide or alkali metal salt, preferably the sodium or chloride salt. (III) may be introduced to give water-soluble (I) (specifically at **polyol** OH group to acid repeating unit molar ratio of 0.6-6 : 1 (preferably 1-3 : 1)), in which case (I) preferably shows a minimum critical dissolution temperature in the range 0-100degreesC in aqueous solution. Alternatively (III) may be introduced to give (I) which are insoluble in water but soluble in non-toxic organic solvents (i.e. esters, ethers, alcohols or ketones (especially acetone, ethyl acetate or ethanol) or their mixtures with water), specifically using chains (III) each having 1-100 (preferably 1-50) hydroxycarboxylic acid repeating units.

L102 ANSWER 18 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-256137 [22] WPIX
DNC C2000-078103
TI Solid formulation for improving bioavailability of poorly water-soluble drugs comprises the drug in an oil and/or fatty acid dispersed in a water-soluble **polyol matrix**.
DC A96 B05 B07
IN LEE, B J
PA (WONJ-N) WON JIN BIOPHARMA CO LTD
CYC 24
PI WO 2000000179 A1 20000106 (200022)* EN 67p A61K009-14 <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA CN JP US
AU 9946556 A 20000117 (200026) A61K009-14 <--
KR 2000006503 A 20000125 (200063) A61K009-10
ADT WO 2000000179 A1 WO 1999-KR341 19990628; AU 9946556 A AU 1999-46556 19990628; KR 2000006503 A KR 1999-24437 19990626
FDT AU 9946556 A Based on WO 200000179
PRAI KR 1999-24437 19990626; KR 1998-24563 19980627
IC ICM A61K009-10; **A61K009-14**
ICS A61K009-107; A61K009-16; A61K009-20; A61K009-48; A61K031-20; A61K038-00

AB WO 200000179 A UPAB: 20000508
NOVELTY - A solid dispersed formulation for poorly water-soluble drugs is made by dispersing the drug in an oil and/or fatty acid and mixing the dispersion with a water-soluble **polyol** matrix and drying the mixture.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for medicines prepared using the novel solid.
USE - The composition is useful for enhancing the bioavailability of poorly water-soluble drugs.
ADVANTAGE - The novel composition provides improved solubility in the gastrointestinal tract giving a great increase in bioavailability. Formulation does not require the use of organic solvents.
Dwg.0/5
FS CPI
FA AB; DCN
MC CPI: A12-V01; B01-C03; B01-D01; B02-P02; B04-B01B; B04-B01C; B04-C01; B04-C01C; B04-C02A; B04-C03; B06-A01; B06-D01; B06-D02; B06-D03; B06-D05; B06-F05; B07-A02; B07-A04; B07-D01; B07-D04C; B07-D05; B07-D09; B07-D13; B10-B04; B10-C03; B10-C04; B10-C04A; B10-C04E; B10-E02; B10-E04C; B10-J02; B12-M11D; B12-M11G
TECH UPTX: 20000508
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The oil is preferably alpha-bisabolol, stearyl glycerrhetinate, salicylic acid, tocopheryl acetate, sodium hyaluronate, panthenol, propylene glycol and apple, propylene glycol and pineapple, ivy extract and 1,3-BG, peach leaf extract, hydrolysed soy flour, wheat protein, birch extract and 1,3-BG, burdock extract and 1,3-BG, liposomes, phosphatidyl cholines, glyceryl stearate, caprylic/capric triglyceride, cetyl octanolate, isopropyl myristate, 2-ethylene isopelagonate, di-C12-13 alkyl malate, ceteatyl (sic) octanoate, butylene glycol dicaprylate/dicaprate, isononyl isostearate, isostearyl isostearate, coco-caprylate/caprate, cetyl octanoate, octyldodecyl myristate, cetyl esters, C10-30 cholesterol/lanosterol ester, hydrogenated castor oil, monoglyceride, diglyceride, triglyceride, beeswax, carnauba wax, suctose (sic) distearate, PEG-8 beeswax, ceresin, ozokerite, macadamia ternifolia nut oil, hydrogenated hi-erucic acid rape seed oil, olive oil, jojoba oil, hybrid sunflower oil, dog rose lips oil, mineral oil, squalene, squalane, medium chain glyceride, myglyol, cremophor, corn oil, perilla oil, cotton seed oil or lipid-soluble vitamin. The fatty acid is preferably oleic acid, cetyl alcohol, stearyl alcohol, stearic acid, myristic acid, linoleic acid, lauric acid or isopropyl myristate. The water-soluble polymer matrix is preferably polyethylene glycol, carbowax or polyvinyl pyrrolidone and may be used in combination with another water-soluble matrix, e.g. gelatin, gum, **carbohydrate**, cellulose, polyvinyl alcohol, polyacrylic acid, inorganic compound, hydroxypropylmethylcelluloseacetyl succinate, shellac, zein, polyvinyl acetate phthalate, Eudragit L100, Eudragit S100, sodium arginate or poly-L-lysine. The oil or fatty acid may include a surfactant, especially glyceryl stearate, polysorbate 60, polysorbate 80, sorbitan trioleate, sorbitan sesquioleate, sorbitan stearate, PEG-20 glyceryl isostearate, ceteth-25, PEG-60, PEG-60 hydrogenated castor oil, nonoxynol-15, PEG-6-decyltetradeceth-20, dimethicone copolyol, glyceryl diisostearate, ceteth-24, cetearyl alcohol, polyoxylethylene nonyphenyl ether, PEG-40 hydrogenated castor oil, cetyl dimethicone copolyol, polyglyceryl-3-methylglucose distearate, PEG-100 stearate, sorbitan isostearate, sodium lauryl glutamate, disodium cocoamphodiacetate, lauric acid diethanolamide, coconut fatty acid diethanolamide, N,N-bis-(2-hydroxyethyl)-cocomide or cocoamidopropyl betaine.
Preferred Drugs: The drug is preferably ketoconazole, itraconazole, cyclosporine, cisapride, acetaminophen, aspirin, acetylsalicylic acid, indomethacin, naproxen, warfarin, papaverine, thiabendazole, miconazole, cinnarizine, doxorubicin, omeprazole, cholecalciferol, melphalan, nifedipine, digoxin, benzoic acid, tryptophan, tyrosine, phenylalanine, aztreonam, ibuprofen, phenoxymethylpenicillin, thalidomide, methyltestosterone, prochlorperazine, hydrocortisone, dideoxypurine nucleoside, vitamin D2, sulfonamide, sulfonylurea, p-aminobenzoic acid,

melatonin, benzylpenicillin, chlorambucil, diazepin, digitoxin, hydrocortisone butyrate, metronisazole benzoate, tolbutamide, prostaglandin E1, fludrocortisone, griseofulvin, miconazole nitrate, leukotriene B4 antagonist, propranolol, theophylline, flubiprofen, sodium benzoate, riboflavin, benzodiazepine, phenobarbital, glyburide, sulphadiazine, sulphaethylthiadiazole, sodium diclofenac, aceclofenac, phyniroin, hioridazine hydrochloride, bropirimine, hydrochlorothiazide, fluconazole, acyclovir, bucillamine, ciprofluoxacin, acetyl-L-carnitine, baclofen, sodium alendronate, lovocarnitine, nimodipine or nimodifine, atenolol, provastatin sodium, lovastatin, isotretinoin, etidronate disodium, doxifluridine, fosfomycin calcium, sotepine, epinastine hydrochloride, carvedilol, fosinopril, trandolapril, etretinate cap, metergoline, mercaptopurine, vancomycin hydrochloride, cefixime, cefuroxim axetil, dirithramycin or dadanosin.

L102 ANSWER 19 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-128217 [12] WPIX
CR 1996-485453 [48]; 2000-258667 [19]
DNC C2000-039344
TI Solid composition comprises non-**amorphous** form of metoprolol and polyethylene oxide.
DC A96 B05 B07
IN SETH, P; STAMM, A
PA (PHAR-N) PHARMA PASS LLC; (SETH-I) SETH P; (STAM-I) STAMM A
CYC 30
PI EP 974343 A1 20000126 (200012)* EN 9p A61K009-20
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
NO 9903588 A 20000124 (200015) A61K031-05
CZ 9902560 A3 20000216 (200016) A61K009-22
SK 9900965 A3 20000214 (200020) A61K009-20
US 6048547 A 20000411 (200025) A61K009-14 <--
HU 9902351 A2 20001228 (200111) A61K031-138
ADT EP 974343 A1 EP 1999-202373 19990719; NO 9903588 A NO 1999-3588 19990722; CZ 9902560 A3 CZ 1999-2560 19990716; SK 9900965 A3 SK 1999-965 19990716; US 6048547 A Cont of WO 1996-FR574 19960415, CIP of US 1997-943304 19971014, US 1998-120914 19980722; HU 9902351 A2 HU 1999-2351 19990712
PRAI EP 1998-402192 19980904; US 1998-120914 19980722; WO 1996-FR574 19960415; US 1997-943304 19971014
IC ICM **A61K009-14**; A61K009-20; A61K009-22; A61K031-05; A61K031-138
ICS A61K031-135
AB EP 974343 A UPAB: 20010224
NOVELTY - A solid composition comprises:
(a) 1-70 % metoprolol (M) in a non-**amorphous** form;
(b) 10-95 % polyethylene oxide (PEO); and
(c) a balance of conventional additives, excluding basic components.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the preparation of the above composition, comprising:
(i) mixing the dry state and the metoprolol (M) and the polyethylene oxide (PEO) and optionally one or more additives;
(ii) optionally adding a solvent, followed by mixing;
(iii) granulating the mixture;
(iv) drying the granules;
(v) optionally adding one or more additives with mixing in the dry state and passing it through a sieve;
(vi) optionally adding one or more additives and mixing in the dry state;
(vii) compressing the mixture obtained into a pressed tablet; and
(viii) optionally coating the compressed tablet.
ACTIVITY - None given.
MECHANISM OF ACTION - None given.
USE - The composition gives a solid composition comprising polyethylene oxide and metoprolol in a specific form.
Dwg.0/0
FS CPI
FA AB; DCN

MC CPI: A05-H03; A12-V01; B03-F; B04-C02A; B04-C03C; B10-A07; B10-B03B; B12-M10
TECH UPTX: 20000308
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition:
Metoprolol (M) is in the form of metoprolol tartrate.
The composition comprises:
(a) 5-45 % (M);
(b) 25-70 % polyethylene oxide (PEO); and
(c) a balance of conventional additives, excluding basic components.
The PEO has a molecular weight of 50000-8000000 (preferably 100000-3000000). The balance consists of e.g. microcrystalline cellulose, **lactose**, ascorbic acid, pigments, plasticizing agents and lubricants. The composition is additionally coated.
Preparation:
The granulation is carried out by passing it through a sieve. The solvent used is an alcohol.
The process comprises:
(i) mixing (M) and optionally one or more additives with an aqueous solution; and then
(ii) adding PEO and mixing again.
The mixing in step (i) is carried out in excess liquid. The process also comprises a granulation step, especially on a screen of a mesh sieve and/or fluidized bed granulator. The process also comprises a drying step. The process also comprises a compression step. The compression step is preceded by a step to add and blend the additives.
The preparation of the composition, comprises:
(i) mixing (M) and optionally one of several additives, with an aqueous solution;
(ii) adding PEO and mixing;
(iii) granulating the mixture;
(iv) drying the granules;
(v) optionally adding one or more additives with mixing in the dry state;
(vi) compressing the mixture into a tablet.
Step (i) comprises mixing the aqueous solution in the presence of excess liquid. The granulation and drying steps are combined in a fluidized bed granulator.
Preparation of the composition, comprises:
(i) mixing the active ingredient, and optionally one or more additives, with an aqueous solution;
(ii) granulating the mixing from (i);
(iii) optionally drying the granules;
(iv) adding PEO and optionally one or more additives; and
(v) compressing the mixture into a tablet.

L102 ANSWER 20 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-089740 [08] WPIX
DNC C2000-025123
TI **Micronization** of medicaments to improve homogeneity and bioavailability of active compound.
DC B07
IN GUERRY, A; LOUZIER, R
PA (GUER-I) GUERRY A; (LOUZ-I) LOUZIER R
CYC 1
PI FR 2779347 A1 19991210 (200008)* 6p A61K031-215
ADT FR 2779347 A1 FR 1998-7057 19980605
PRAI FR 1998-7057 19980605
IC ICM A61K031-215
ICS **A61K009-14**; B01F011-02
AB FR 2779347 A UPAB: 20000215
NOVELTY - The micronization of medicaments comprises micronizing fenofibrate (isopropyl 2-(4-(4-chlorobenzoyl)-phenoxy)-2-methyl-propionate) in a tank (1) under resonance by a passive oscillating system comprising a mechanical vibrator (5), a parabolic reflector (10) on a spring (11), a periodic emitter (9) activated by generators (8) and (6).
USE - Useful for micronizing pharmaceutical formulations, especially capsules comprising fenofibrate.

ADVANTAGE - The formulation has an improved homogeneity and fenofibrate has an improved bioavailability in vivo.

DESCRIPTION OF DRAWING(S) - The drawing shows a schematic view of the apparatus for preparing the fenofibrate capsules.

Tank 1
Inlet pipes 2-4
Mechanical vibrator 5
Generators 6,8
Outlet pipe 7
Periodic emitter 9
Parabolic reflector 10
Dwg.1/1

FS CPI
FA AB; GI; DCN
MC CPI: B10-F02; B11-C05; B12-M11C
TECH UPTX: 20000215

TECHNOLOGY FOCUS - MECHANICAL ENGINEERING - Preferred Apparatus: Pipes (2), (3) and (4) are connected to the tank (1) to feed the fenofibrate which will be micronized by the passive oscillating system (3), the parabolic reflector (10) and the periodic emitter (9), in order to obtain fenofibrate particles of less than 1 microns. Monohydratred **lactose** (1 %) and starch (0.3 %) are added to the micronized fenofibrate and the mixture was granulated with water (8.9 %) in the tank (1). The mixture is dried and calibrated into granules of less than 1000 microns. Polyvinylpyrrolidone and magnesium stearate are added. The obtained homogenized powder is discharged from the tank (1) though the pipe (7), dried and placed into capsules.

L102 ANSWER 21 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-086664 [07] WPIX
DNC C2000-024112
TI Thermoprotected microparticle compositions, such as lyophilized or spray dried powder for **parenteral** administration.
DC B07 C07
IN MISHRA, A K
PA (RTPP-N) RTP PHARMA INC
CYC 86
PI WO 9961001 A1 19991202 (200007)* EN 25p A61K009-14 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
AU 9942175 A 19991213 (200020) A61K009-14 <--
SE 2000004312 A 20010118 (200112) A61K009-51
EP 1079808 A1 20010307 (200114) EN A61K009-14 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9961001 A1 WO 1999-US11888 19990528; AU 9942175 A AU 1999-42175 19990528; SE 2000004312 A WO 1999-US11888 19990528, SE 2000-4312 20001124; EP 1079808 A1 EP 1999-926001 19990528, WO 1999-US11888 19990528
FDT AU 9942175 A Based on WO 9961001; EP 1079808 A1 Based on WO 9961001
PRAI US 1998-87331 19980529
IC ICM **A61K009-14**; A61K009-51
ICS A61K009-50
AB WO 9961001 A UPAB: 20000209

NOVELTY - Compositions of submicron to micron sized particulate suspension of water-insoluble or poorly water-soluble pharmaceutical agents containing a water soluble polyhydroxy compound can be autoclaved without any marked increase of mean particle size.

DETAILED DESCRIPTION - An aqueous suspension composition of water insoluble or poorly soluble active substance together with at least one surface modifier and a water soluble polyhydroxy thermoprotecting agent is subsequent to terminal steam sterilization. The ratio of active substance to surface modifier and thermoprotecting agent selected to provide particle size stability during and after terminal steam sterilization,

provided that the particle size is not more than twofold increase in the volume weighted mean particle size of the particulate aqueous suspension.

USE - The invention is used for **parenteral** administration preferably intramuscular or subcutaneous (claimed).

ADVANTAGE - The composition can be autoclaved without any marked increase of mean particle size. The composition withstood the stresses that are usually known to promote particle size growth or flocculation or agglomeration. These compositions can be successfully lyophilized before or after steam sterilization. In addition, the lyophilized preparations can be reconstituted by addition of water to make an aqueous suspension having qualities similar to the original suspension. These compositions did not use any surfactants that would require cloud point modifying molecules for protection against coagulation, flocculation, crystal growth, or particle size growth during the terminal steam sterilization process.

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B01-D01; B04-C01C; B04-C02C; B04-N03A; B07-H; B10-A07; B12-M07; B12-M11G; B14-A04; B14-G02; C01-D01; C04-C01C; C04-C02C; C04-N03A; C07-H; C10-A07; C12-M07; C12-M11G; C14-A04; C14-G02
TECH UPTX: 20000209

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Process: The pH of the suspension before terminal steam sterilization is 5-9 provided that the pH value prior to terminal steam sterilization is selected such that the chemical stability of the suspension components is maintained during and after the terminal steam sterilization.

Preferred Composition: The composition also includes a non-surfactants additive such that, on diluting the formulation with a diluent suitable for **parenteral** administration, a suitable osmotic pressure of the diluted suspension results. The surface modifier provides drug to surface modifier ratio of up to 5:1. The surface modifier is present at 0.2-5 weight % (wt. %). The composition also contains pharmaceutical excipients for ophthalmic, peroral, or transdermal administration of the water insoluble or poorly soluble active drug substance.

Preferred Modifiers: One or more of the surface modifiers are natural phopholipids or synthetic phospholipids, preferably, egg phospholipid or soy phospholipid.

Preferred Drugs: The active substance is an antifungal agent, itraconazole, an immuno-suppressive drug (preferably cyclosporin), sterol (preferred alfaxalone).

TECHNOLOGY FOCUS - POLYMERS - Preferred Agent: The thermoprotecting agent is a water soluble polyhydroxy compound from **trehalose, lactose**, dextrose, **sorbitol, dextran, trehalose**, and **mannitol**.

L102 ANSWER 22 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-023475 [02] WPIX
DNC C2000-005787
TI Formulation of paroxetine, with polymers to provide a solid dispersion.
DC A96 B02
IN CHANG, S; HEIN, W A; KAO, H D
PA (ENDO-N) ENDO PHARM INC
CYC 86
PI WO 9956751 A1 19991111 (200002)* EN 36p A61K031-445
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
ZA 9903081 A 20000126 (200011) 35p A61K000-00
AU 9937876 A 19991123 (200016)
US 6168805 B1 20010102 (200103) A61K009-14 <--
EP 1075263 A1 20010214 (200111) EN A61K031-445

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9956751 A1 WO 1999-US9835 19990505; ZA 9903081 A ZA 1999-3081 19990504; AU 9937876 A AU 1999-37876 19990505; US 6168805 B1 US 1998-74355 19980507; EP 1075263 A1 EP 1999-920358 19990505, WO 1999-US9835 19990505
FDT AU 9937876 A Based on WO 9956751; EP 1075263 A1 Based on WO 9956751
PRAI US 1998-74355 19980507
IC ICM A61K000-00; **A61K009-14**; A61K031-445
ICS A61K009-20
AB WO 9956751 A UPAB: 20000112
NOVELTY - Preparation of solid, **amorphous** paroxetine, by mixing the drug as free base or salt with a polymer, and drying to form a solid composition; followed optionally by mixing with an excipient and tabletting. Paroxetine is the generic name for (-)-trans-40(4'-fluorophenyl)-3-(3',4'-ethylenedioxyphenoxymethyl)piperidine.

ACTIVITY - Antidepressant.

MECHANISM OF ACTION - Paroxetine is a known serotonin serial reuptake inhibitor (SSRI).

USE - The composition is used for treatment of depression. In addition to humans, warm blooded animals in general are mentioned.

ADVANTAGE - The formulation with polymer provides an improved and more convenient dosage form than prior art. Paroxetine itself is a viscous oil with poor water solubility; paroxetine hydrochloride is hygroscopic with poor handling properties, although the hemihydrate is more amenable.

Dwg.1/12
FS CPI
FA AB; GI; DCN
MC CPI: A12-V01; B04-C02A; B07-D05; B14-J01A1; B14-J03
TECH UPTX: 20000112
TECHNOLOGY FOCUS - POLYMERS - Preferred Components: The polymer is water soluble, at least partially. Immediate release formulations of the drug are preferred, so that the chosen polymer should not control or delay release of the paroxetine. These undesired polymers include insoluble, water swellable, fibrous cross-linked carboxy functional types, e.g., calcium polycarbophil. Suitable polymers are polyvinylpyrrolidone (PVP), hydroxypropyl methylcellulose, hydroxypropyl cellulose, block copolymers of ethylene and propylene oxide, and polyethylene glycol, most preferably PVP, with average molecular weight 2.5-3000 kiloDaltons. Polymeric excipients include cellulose and its derivatives, croscarmellose sodium, crospovidone, dextrates, dextrin, maltodextrin, starch, and guar gum.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Components: Inorganic excipients are calcium carbonate, phosphate, and sulfate.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: Organic excipients are dextrose, **fructose**, **lactose**, **mannitol**, **sorbitol**, xylitol, and **sucrose**.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: A preferred salt of paroxetine is the hydrochloride. Preferred Process: Weight ratios of polymer to paroxetine are from 0.4:1 to 20:1. For preferred water soluble polymers, an aqueous solution of drug and polymer is formed on or after mixing; conveniently, the paroxetine is added as the normal available free base form, and an acid, preferably hydrochloric, is added, in mole ratio from 1:1 to 1:1.8, to convert the paroxetine to soluble salt and obtain a clear solution. Mixing is optionally at elevated temperatures, 25-100degreesC, most preferably at about 60degreesC. The resultant solution or dispersion is then dried; spray drying on to a substrate, e.g., calcium phosphate excipient, is suggested.

L102 ANSWER 23 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-443859 [37] WPIX
DNC C1999-130683
TI Lyophilization of solutions by freezing to temperature between eutectic temperature and glass transition temperature followed by sublimation.
DC A14 A96 B07
IN AUFFRET, A

PA (AUFF-I) AUFFRET A
CYC 84
PI WO 9930688 A1 19990624 (199937)* EN 145p A61K009-14 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD
GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV
MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
UA UG US UZ VN YU ZW
AU 9915701 A 19990705 (199948) A61K009-14 <--
ADT WO 9930688 A1 WO 1998-GB3747 19981214; AU 9915701 A AU 1999-15701 19981214
FDT AU 9915701 A Based on WO 9930688
PRAI GB 1997-26343 19971213
IC ICM **A61K009-14**
ICS A61K009-19; A61K047-02
AB WO 9930688 A UPAB: 19990914
NOVELTY - Freezing solutions to a temperature between the glass transition temperature and the eutectic temperature for lyophilizing.

DETAILED DESCRIPTION - Lyophilizing a solution comprises freezing to a temperature at or below the lower of its eutectic temperature (ET) or its glass transition temperature (TG) and removing at least a portion of the solvent by sublimation in a first drying stage, the solution containing an accelerant excipient to enhance the rate of solvent sublimation.

INDEPENDENT CLAIMS are included for the following:

(a) lyophilization of a solution for storage comprising freezing to a temperature at or below the lower of its ET or its TG and removing solvent by sublimation, the solution comprising a substance capable of raising the TG of the lyophilized solution above the ambient storage temperature;

(b) lyophilizing an aqueous solution of a glass-forming substance comprising freezing to a temperature at or below the lower of ET and TG and removing at least a portion of solvent by sublimation in a first drying stage, the solution containing an ammonium salt comprising ammonium formate, ammonium acetate or ammonium bicarbonate;

(c) a method of manufacturing a rapidly dissolving dosage form of a pharmaceutically active compound comprising lyophilizing a solution of the compound as above;

(d) a method of preparing a sterile solution of a drug for oral or **parenteral** administration comprising adding sterile water to a sterile rapidly dissolving dosage form obtained as above;

(e) a lyophilized product obtained as above.

USE - The methods are used for stabilization of solutions for storage.

ADVANTAGE - The accelerant enhances the rate of solvent sublimation and the method overcomes the need for subsequent drying steps.

DESCRIPTION OF DRAWING(S) - The figure shows the comparative sublimation rates, achieved by the formulation of 8.5% solutions of **sucrose**, PVP or **lactose** each containing TBA or one or several other volatile excipients, as percent weight losses with time.

Dwg.1a/35
FS CPI
FA AB; GI; DCN
MC CPI: A04-D05A; A12-V01; B04-C03B; B05-C01; B05-C04; B06-D01; B06-D09; B07-A02A; B07-A02B; B12-M11G
TECH UPTX: 19990914
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Method: The solution comprises a substance capable of forming a glass on freeze concentration and comprises at least one non-volatile substance and a pharmaceutically active substance. All or a portion of the solvent is removed during the sublimation step and the method further comprises a secondary drying stage after the sublimation step to remove excess solvent. The lyophilized solution is stable at ambient temperature and/or pressure and has a TG higher than ambient temperature and/or pressure under desired storage conditions. The solvent is aqueous and the solution undergoes ice sublimation during lyophilization. The accelerant excipient, in whole or in part, undergoes eutectic crystallization on cooling or is included in

the **amorphous** state. The accelerant excipient is at least partly removed during sublimation or is not removed during sublimation and comprises an inorganic salt. The accelerant excipient is an ammonium salt of a weak or poorly dissociated acid, preferably ammonium formate, ammonium acetate or ammonium bicarbonate and is present in combination with at least one of **sucrose**, PVP or **lactose**.
In method (a) no additional drying step is required after sublimation and the substance is capable of forming a matrix to support the **amorphous** phase during sublimation. The solution is aqueous and undergoes ice sublimation during lyophilization and the solution contains a substance capable of forming a colloidal solution in water. The solution contains a hydrophilic polymer, preferably polyvinylpyrrolidone.
In method (b) the solution further comprises a bulking agent comprising PVP, **sucrose** or **lactose**.
In method (c) the solution contains an accelerant excipient which is pharmacologically acceptable and which is volatile and removed during sublimation. The solution further comprises a bulking agent as above.
In method (d) the solution is frozen to a temperature just below or about TG or its ET, preferably at a temperature of within 15degreesC of the lower of its ET and TG, particularly within 10degreesC, especially within 5degreesC. Preferred Product: The lyophilized product is rapidly dissolvable and the product does not require additional drying steps. The TG of the product is higher than ambient storage temperatures, preferably by at least 10degreesC. The lyophilized product is a pharmaceutical composition, preferably containing an active agent comprising Eletriptan, Sildenafil or Viagra. The composition further comprises at least one of PVP, **Sucrose**, **lactose**, ammonium bicarbonate or ammonium acetate.

L102 ANSWER 24 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-337447 [28] WPIX
DNC C1999-099193
TI New particle consists of a solid dispersion of lipid lowering agent and one or more water-soluble polymers, for treatment of atherosclerosis.
DC A96 B03
IN BAERT, L; VERRECK, G
PA (JANC) JANSSEN PHARM NV
CYC 84
PI WO 9922738 A1 19990514 (199928)* EN 44p A61K031-495
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9911576 A 19990524 (199940)
EP 1028730 A1 20000823 (200041) EN A61K031-495
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
NO 2000002279 A 20000428 (200042) A61K000-00
ZA 9809997 A 20000726 (200042) 43p A61K000-00
CZ 2000001487 A3 20000816 (200048) A61K031-496
BR 9814109 A 20001003 (200053) A61K031-495
SK 2000000597 A3 20001211 (200103) A61K031-495
CN 1278175 A 20001227 (200123) A61K031-495
NZ 503413 A 20010629 (200140) A61K009-14 <--
ADT WO 9922738 A1 WO 1998-EP6998 19981027; AU 9911576 A AU 1999-11576 19981027; EP 1028730 A1 EP 1998-954483 19981027, WO 1998-EP6998 19981027; NO 2000002279 A WO 1998-EP6998 19981027, NO 2000-2279 20000428; ZA 9809997 A ZA 1998-9997 19981102; CZ 2000001487 A3 WO 1998-EP6998 19981027, CZ 2000-1487 19981027; BR 9814109 A BR 1998-14109 19981027, WO 1998-EP6998 19981027; SK 2000000597 A3 WO 1998-EP6998 19981027, SK 2000-597 19981027; CN 1278175 A CN 1998-810808 19981027; NZ 503413 A NZ 1998-503413 19981027, WO 1998-EP6998 19981027
FDT AU 9911576 A Based on WO 9922738; EP 1028730 A1 Based on WO 9922738; CZ 2000001487 A3 Based on WO 9922738; BR 9814109 A Based on WO 9922738; NZ

503413 A Based on WO 9922738
PRAI EP 1997-203407 19971103
IC ICM A61K000-00; **A61K009-14**; A61K031-495; A61K031-496
ICS A61J000-00; A61K009-10; A61K031-41; A61K031-443; A61K031-4439; A61K031-444; A61K031-506; A61P003-04; A61P003-06; A61P009-10
AB WO 9922738 A UPAB: 19990719
NOVELTY - A new particle consists of a solid dispersion comprising a lipid lowering agent and one or more water-soluble polymers.
DETAILED DESCRIPTION - A new particle consists of a solid dispersion comprising a lipid lowering agent and one or more water-soluble polymers.
The lipid lowering agent is of formula (I), disclosed in WO9613499, its N-oxide, isomers or salts:

A+B = N=CH, CH=N, CH2CH2, CH=CH, COCH2 or CH2CO, optionally substituted by 1-2 1-6C alkyl;
R1 = H, 1-6C alkyl or halo;
R2 = H or halo;
R3 = H, 1-8C alkyl (optionally substituted by OH, oxo, 3-6C cycloalkyl or aryl) or 3-6C cycloalkyl;
Het = pyridine or pyrimidine (each optionally substituted by 1-2 1-6C alkyl, hydroxy, 1-6C alkyloxy, trihalomethyl, amino, mono- or di(1-6C alkyl)amino or aryl), tetrazole (optionally substituted by 1-6C alkyl or aryl), triazole, thiadiazole, oxadiazole, imidazole, thiazole or oxazole (all optionally substituted by 1-2 1-6C alkyl, hydroxy, 1-6C alkyloxy, trihalomethyl, amino or mono- or di(1-6C alkyl)amino));
aryl = phenyl optionally substituted by 1-6C alkyl or halo.
An INDEPENDENT CLAIM is included for a pharmaceutical package suitable for commercial sale comprising a container, an oral dosage form of lipid lowering agent and written matter non-limited as to whether the dosage form can be taken with or without food.
ACTIVITY - Antilipemic.
In an apolipoprotein B inhibition test, the compound of formula A had an IC50 of 2.3 x 10-8M.
MECHANISM OF ACTION - None given.
USE - The particles are useful in a pharmaceutical dosage form for immediate release of a lipid lowering agent on oral ingestion for treatment of hyperlipidemia, obesitas or atherosclerosis.
Dwg.0/0
FS CPI
FA AB; GI; DCN
MC CPI: A12-V01; B04-C02; B04-C03B; B07-A04; B07-D11; B07-D13; B14-E12; B14-F06; B14-F07
TECH UPTX: 19990719
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred composition: The particle size is less than 850 microns. The lipid lowering agent is in a non-crystalline phase. The solid dispersion is in the form of a solid solution comprising the lipid lowering agent and the polymer, or in the form of a dispersion in which **amorphous** or microcrystalline lipid lowering agent or **amorphous** or microcrystalline polymer is dispersed evenly in a solid solution comprising the lipid lowering agent and the polymer. The weight-by-weight ratio of lipid lowering agent to polymer is 1:1 to 1:35. Preferably the particle consists of a solid solution comprising lipid lowering agent (1 part by weight) and hydroxypropyl methylcellulose HPMC 2910 mPa.s (1-3 parts by weight) obtained by blending the components, extruding the blend at 120-300 degreesC, grinding the extrudate and optionally sieving the particles. The particle further comprises one or more pharmaceutical excipients. Preferred components: The water-soluble polymer has an apparent viscosity of 1-100 mPa.s when dissolved in a 2% aqueous solution at 20 degreesC and is selected from alkylcellulose (such as methylcellulose), hydroxyalkylcellulose (such as hydroxymethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose and hydroxybutylcellulose), hydroxyalkyl alkylcellulose (such as hydroxyethyl methylcellulose and hydroxypropyl methylcellulose), carboxyalkylcellulose (such as carboxymethylcellulose), alkali metal salts of carboxyalkylcellulose (such as sodium carboxymethylcellulose), carboxyalkylalkylcellulose (such as

carboxymethylethylcellulose), carboxyalkylcellulose esters, starch, pectin (such as sodium carboxymethylamylopectin), chitin derivatives (such as chitosan), **polysaccharides** (such as alginic acid and its alkali metal and ammonium salts), carrageenans, galactomannans, traganth, agar-agar, gummi arabicum, guar gummi and xanthan gummi, polyacrylic acids and their salts, polymethacrylic acids and their salts, methacrylate copolymers, polyvinyl alcohol, polyvinylpyrrolidone and its copolymers with vinyl acetate, polyalkylene oxides such as polyethylene oxide and polypropylene oxide and copolymers of ethylene oxide and propylene oxide. Preferably the water-soluble polymer is hydroxypropyl methylcellulose HPMC 2910 5 mPa.s.

Preparation: The particle is obtained by melt-extrusion of the components, grinding and optionally sieving. The components are blended, the blend is extruded at 120-300 degreesC, the extrudate is ground and the particles are optionally sieved.

L102 ANSWER 25 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-256498 [22] WPIX
CR 1999-256497 [22]
DNN N1999-191131 DNC C1999-075220
TI Process for the manufacture of dry, **amorphous** products comprising biologically active material.
DC B04 B05 B07 D16 Q76
IN GABEL, R; MATTERN, M; WINTER, G; WIRL, A; WOOG, H
PA (HOFF) ROCHE DIAGNOSTICS GMBH
CYC 25
PI EP 913178 A1 19990506 (199922)* EN 23p B01D001-18
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT EP 913178 A1 EP 1998-120455 19981029
PRAI EP 1997-119112 19971103
IC ICM B01D001-18
ICS **A61K009-14**; F26B003-02
AB EP 913178 A UPAB: 19990609
NOVELTY - Process for the manufacture of dry, **amorphous** products comprising biologically active material by means of convection drying and products obtainable by the process.

DETAILED DESCRIPTION - Process for the manufacture of dry, **amorphous** products comprising biologically active material, in particular therapeutically active material, contain substance mixtures for stabilization, characterized in that a solution or suspension of biological material and a substance mixture consisting of:

(a) a **carbohydrate** and at least one zwitter ion with polar or apolar radical or derivatives thereof;

(b) at least two zwitter ions with polar or apolar radicals or derivatives thereof; and/or

(c) at least one zwitter ion with polar or apolar radical or a plurality of zwitter ions with polar or apolar radicals or derivatives thereof

is produced and dried by means of convection drying with adjustment of a relative moisture content of less than 70% in the stationary phase at an inlet air temperature of 50-300 deg. C.

An INDEPENDENT CLAIM is also included for the use of the substance mixtures above for stabilization of biologically active material.

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - The **amorphous** products are used for producing diagnostic or therapeutic compositions.

ADVANTAGE - The manner of the drying process proves to be particularly advantageous in relation to the stability of the biological materials in the formulations and ensures yields greater than 90 deg. C.

Dwg.0/0
FS CPI GMPI
FA AB; DCN
MC CPI: B04-D02; B04-L01; B04-N02; D05-A02; D05-H09
TECH UPTX: 19990609

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred conditions: The solution or suspension is prepared at a specific pH, preferably a pH of 7.0-7.5, before the convection dry.
The drying takes place by fluidized drying, lift air or flight drying (preferably spray or fluidized bed drying).
Preferred zwitter ions: The preferred zwitter ions with polar or apolar radicals are amino carboxylic acids.
Preferred **carbohydrates**: The **carbohydrate** is mono-, oligo-, **polysaccharides**, arginine, aspartic acid, citrulline, glutamic acid, histidine, lysine, acetylphenylalanine ethyl ester, alanine, cysteine, glycine, isoleucine, leucine, methionine, phenylalanine, tryptophan, valine and/or derivatives thereof.
The substance mixtures employed in (b) comprise arginine, aspartic acid, citrulline, glutamic acid, histidine, lysine, acetylphenylalanine ethyl ester, alanine, cysteine, glycine, isoleucine, leucine, methionine, phenylalanine, tryptophan, valine and/or there derivatives.
The substance mixtures employed in (c) are the salts of the zwitter ions.
Preferred conventional ancillary substances added to the solution include buffers, surfactants, antioxidants, isotonicizing agents and preservatives.

TECHNOLOGY FOCUS - BIOLOGY - Preferred biological material: The preferred biological material employed is one or more substances of the groups of proteins, peptides, glycoproteins, lipoproteins, enzymes, coenzymes, antibodies, antibody fragments, virus constituents, cells and cell constituents, **vaccines**, DNA, RNA, biological therapeutic and diagnostic agents or their derivatives.
TECHNOLOGY FOCUS - PHARMACEUTICALS - The product obtained is an **amorphous**, microscopically homogenous product containing a biologically active material and a substance mixture for stabilization, with a glass transition temperature at least20degreesC (preferably at least40degreesC) and a residual moisture content less than8% (g/g) (preferably less than4% (g/g).
The **amorphous** product obtained are in the form of powders in a particle size range 0.0005-1 (preferably 0.001-0.1) mm.

L102 ANSWER 26 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-204412 [17] WPIX
DNC C1999-059469
TI Co-precipitate comprising cefuroxime axetil and water soluble excipient - used as broad spectrum antibiotic.
DC B02
IN SHERMAN, B C
PA (SHER-I) SHERMAN B C
CYC 83
PI WO 9908683 A1 19990225 (199917)* EN 17p A61K031-545
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9888470 A 19990308 (199929) A61K031-545
CA 2209868 A 19990215 (199931) A61K031-545
EP 996449 A1 20000503 (200026) EN A61K031-545
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9908683 A1 WO 1998-CA773 19980807; AU 9888470 A AU 1998-88470 19980807; CA 2209868 A CA 1997-2209868 19970815; EP 996449 A1 EP 1998-940001 19980807, WO 1998-CA773 19980807
FDT AU 9888470 A Based on WO 9908683; EP 996449 A1 Based on WO 9908683
PRAI CA 1997-2209868 19970815
IC ICM A61K031-545
ICS **A61K009-14**; A61K009-20
AB WO 9908683 A UPAB: 19990503
NOVELTY - Co-precipitate comprising cefuroxime axetil and a water-soluble excipient provides an oral composition with increased bioavailability.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) production of the above co-precipitate which comprises dissolving axetil and water soluble excipient in at at least 1 solvent and evaporating the solvent and (2) a pharmaceutical tablet comprising the above co-precipitate.

USE - Cefuroxime axetil is a wide spectrum antibiotic.

ADVANTAGE - The co-precipitate provides cefuroxime axetil in an oral form has good bioavailability. The co-precipitate allows use of **amorphous** or crystalline cefuroxime axetil. The co-precipitate has a higher water solubility than cefuroxime axetil alone and so the bioavailability of the co-precipitate is higher even though the disintegration time of the formulation in the digestive tract is slower than prior art products.

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B02-C01; B04-C02A2; **B04-D01**; B07-D03; B10-A07; B12-M10

L102 ANSWER 27 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-142569 [12] WPIX
DNC C1999-041580
TI Entrapping additive agent for e.g. foodstuffs in **carbohydrate** bodies - comprises treating pure untreated spherical **carbohydrate** bodies with fluid comprising non-solubilising additive and entrapping into crystallite spaces.
DC B07
IN BLAKE, A S; FUISZ, R C; YANG, R K
PA (FUIS-N) FUISZ TECHNOLOGIES LTD
CYC 80
PI WO 9904762 A2 19990204 (199912)* EN 28p A61K009-16
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
US 5874110 A 19990223 (199915) A61K009-14 <--
AU 9883981 A 19990216 (199926) A61K009-16
EP 998269 A2 20000510 (200027) EN A61K009-16
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL SE
ADT WO 9904762 A2 WO 1998-US14455 19980713; US 5874110 A US 1997-898306 19970722; AU 9883981 A AU 1998-83981 19980713; EP 998269 A2 EP 1998-934470 19980713, WO 1998-US14455 19980713
FDT AU 9883981 A Based on WO 9904762; EP 998269 A2 Based on WO 9904762
PRAI US 1997-898306 19970722
IC ICM **A61K009-14**; A61K009-16
AB WO 9904762 A UPAB: 19990324
Entrapping an additive agent in **carbohydrate** bodies comprises: (a) treating pure untreated spherical **carbohydrate** bodies (capable of at least partially crystallising from their initial **amorphous** state under equilibrium conditions) with a fluid comprising a non-solubilising additive; and (b) entrapping the additive into crystallite spaces as they are formed on crystallisation of the bodies. Delivery systems obtained by this process are also claimed.

USE - (I) is a simple method of providing inclusion complexes of hydrophobic and non-water soluble additives for addition to foodstuffs and pharmaceuticals without recourse to costly solvents.

ADVANTAGE - The process takes place under ambient conditions providing a cost-effective method of integrating previously difficult ingredients into mixtures under manufacturing conditions. More than one agent can be added at the same time further improving efficiency.

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B04-B01C1; B07-A02; B12-M11E

L102 ANSWER 28 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1998-530830 [45] WPIX
CR 1993-213784 [26]
DNC C1998-159172
TI Treatment of mucosal tissue - comprises administration of a composition comprising a solid **matrix** in which a medicament, preferably an anti-ulcer agent, is suspended.
DC A96 B05
IN FUISZ, R C
PA (FUIS-N) FUISZ TECHNOLOGIES LTD
CYC 1
PI US 5811123 A 19980922 (199845)* 14p A61K009-10
ADT US 5811123 A CIP of US 1991-808599 19911217, Div ex US 1993-113485 19930827, CIP of US 1994-81336 19940614, US 1995-465974 19950606
FDT US 5811123 A CIP of US 5622717, Div ex US 5651987
PRAI US 1995-465974 19950606; US 1991-808599 19911217; US 1993-113485 19930827; US 1994-81336 19940614
IC ICM A61K009-10
ICS **A61K009-14**
AB US 5811123 A UPAB: 19981111
Treatment of mucosal tissue (MT) comprises contacting MT with a composition having rapid delivery and enhanced adhesion to MT comprising a solid matrix in which a medicament is suspended. The matrix is formed by flash-flow melt-spinning a mixture comprising: (a) a carrier (CAR) comprising a **saccharide**; (b) a medicament; and (c) a hydrogel (HG) for providing mucosal adhesion selected from gums, alginates, celluloses, pectins, gelatin and/or polycarbophil. Also claimed is preparation of a composition (A) having a medicament dispersed in a soluble matrix comprising subjecting a feedstock to flash-flow transformation. The feedstock comprises the medicament, HG and a carrier.
USE - The method is particularly useful for the treatment of mouth and stomach ulcers. However, the composition may further include acne preparations, analgesics, antipyretics, antacids, anti-flatulent agents, anthelmintics, antianginals, antianxiety agents, antiarrhythmics, antiarthritics, anticoagulants, anti-thrombolitic agents, anticonvulsants, anti-Parkinson agents, antidepressants, antidiarrhoeals, antifungals, anti-trichomonals, antivirals, antigout agents, antihistamines, antipruritics, antihypertensives, anti-infectives, anti-migraines, antiemetics, antineoplastics, antiulcer agents, anti-reflux agents, antispasmodics, bronchial dilators, antiasthmatics, cardiac agents, contraceptives, hormones, hypolipidaemics, laxatives, tranquillisers, muscle relaxants ophthalmic preparations, mineral supplements, sedatives, hypnotics and/or vitamins.
ADVANTAGE - The adherence and speed of contact of the medicament are improved and so the efficacy of the drug is improved.
Dwg.0/4
FS CPI
FA AB; DCN
MC CPI: A03-A01; A03-C01; A12-V01; B04-B01C1; B04-C02; B04-C02A; B04-C02D; B04-C02X; B14-A01; B14-A02; B14-A03D; B14-A04; B14-B03; B14-C01; B14-C02; B14-C04; B14-C09; B14-D01; B14-E01; B14-E02; B14-E03; B14-E05; B14-E08; B14-E09; B14-F01; B14-F01A; B14-F01D; B14-F02B; B14-F04; B14-F06; B14-H01; B14-J01A1; B14-J01A3; B14-J01B1; B14-J01B2; B14-J01B4; B14-J05A; B14-J05D; B14-J07; B14-K01A; B14-K01D; B14-L09; B14-N03; B14-N05; B14-N17D; B14-P01

L102 ANSWER 29 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1998-348021 [30] WPIX
CR 1994-293954 [36]; 1996-159656 [16]; 1997-331543 [30]; 1997-332006 [30]; 1997-384623 [35]; 1997-456762 [42]; 1997-469491 [43]
DNC C1998-107484
TI Delivery of water insoluble bioactive agents as suspended nanoparticles - by coating agent in organic phase with aqueous protein and/or synthetic polymer as stabiliser, under high shear, notable use for taxol..
DC B05 B07
IN DESAI, N P; LOUIE, L; MAGDASSI, S; SOON-SHIONG, P; TAO, C; YANG, A; YAO, Z; ZHENG, T

PA (VIVO-N) VIVORX PHARM INC
CYC 80
PI WO 9814174 A1 19980409 (199830)* EN 71p A61K009-14 <--
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9745929 A 19980424 (199835)
NO 9901620 A 19990601 (199932) A61K009-14 <--
US 5916596 A 19990629 (199932) A61K009-14 <--
EP 961612 A1 19991208 (200002) EN A61K009-14 <--
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
CN 1237901 A 19991208 (200016) A61K009-14 <--
AU 718753 B 20000420 (200029) A61K009-14 <--
NZ 335133 A 20001222 (200104) A61K009-14 <--
JP 2001501931 W 20010213 (200112) 58p A61K047-30
ADT WO 9814174 A1 WO 1997-US17157 19970924; AU 9745929 A AU 1997-45929 19970924; NO 9901620 A WO 1997-US17157 19970924, NO 1999-1620 19990406; US 5916596 A Div ex US 1993-23698 19930222, CIP of US 1995-412726 19950329, US 1996-720756 19961001; EP 961612 A1 EP 1997-944429 19970924, WO 1997-US17157 19970924; CN 1237901 A CN 1997-199720 19970924; AU 718753 B AU 1997-45929 19970924; NZ 335133 A NZ 1997-335133 19970924, WO 1997-US17157 19970924; JP 2001501931 W WO 1997-US17157 19970924, JP 1998-516657 19970924
FDT AU 9745929 A Based on WO 9814174; US 5916596 A Div ex US 5439686, CIP of US 5560933; EP 961612 A1 Based on WO 9814174; AU 718753 B Previous Publ. AU 9745929, Based on WO 9814174; NZ 335133 A Based on WO 9814174; JP 2001501931 W Based on WO 9814174
PRAI US 1996-720756 19961001; US 1993-23698 19930222; US 1995-412726 19950329
IC ICM **A61K009-14**; A61K047-30
ICS A61J003-00; A61K009-38; A61K045-00; A61K047-48; A61K049-00; A61P029-00; A61P035-00
AB WO 9814174 A UPAB: 20010302
Formulation of a pharmacologically active agent, almost insoluble in water, for in vivo delivery, comprises subjecting a mixture comprising: (a) the agent dispersed in an organic phase; and (b) aqueous medium containing biocompatible polymer; to high shear conditions in a high pressure homogeniser at a pressure between 3000 and 30000 psi, provided that substantially no surfactants are present; and, optionally, removing the organic and/or aqueous phase from the mixture. Also claimed is a drug delivery system, comprising particles of a solid or liquid, water insoluble pharmacologically active agent, coated with protein, in which the coating has associated protein; a portion of the active agent is contained within the protein coating, and a portion is associated with the protein; and the average diameter of the particles is not greater than 1 mu .

USE - The formulation produces microparticles, but preferably nanoparticles, i.e., diameter less than 1 micron, of active agent, coated with the biocompatible polymer, suspended in the aqueous phase. These can be **injected** to provide a pre-programmed release profile, with duration from a few hours to weeks or months from a single dose. Under the high shear conditions, the particles are small enough (less than a few microns) to be safe, without risk of capillary blockage or infarction; smaller sizes (less than 200 nm) can be sterile filtered for **injection**. The particles may be either crystalline and/or **amorphous**, with the latter preferred for better bioavailability. A wide variety of active agents, including therapeutic, prophylactic, and diagnostic agents, and agents of nutritional value, can be delivered in the formulation. Examples of therapeutic/prophylactic agents include analgesics, antipyretics, anaesthetics, antiasthmatics, antibiotics, antidepressants, antidiabetics, antifungals, antihypertensives, antiinflammatories, antineoplastics, antianxiety or antimigraine drugs, immunosuppressives, sedatives, hypnotics, antianginals, antipsychotics,

antimania or antigout agents, antiarrhythmics, antiarthritics, anticoagulants, thrombolytics, antifibrinolytics, haemorheologic or antiplatelet agents, antiparkinson or calcium regulatory agents, antihistamines, antipruritics, antimicrobials, antibacterials, antivirals, antiinfectives, bronchodilators, hormones, , hypoglycaemics, hypolipidaemics, proteins, nucleic acids (both sense and antisense to encode proteins), erythropoietin stimulators, antiulcer, antireflux agents, antinauseants, and antiemetics. Most notable are antineoplastics and immunosuppressants; specific antineoplastic examples are adriamycin, cyclophosphamide, actinomycin, bleomycin, duanorubicin, doxorubicin, epirubicin, mitomycin, methotrexate, fluorouracil, cisplatin, carboplatin, carmustine (BCNU), methyl-CCNU, etoposide, piposulphan, interferon, or camptothecin, taxol (paclitaxel), taxotere, and their derivatives; of immunosuppressants, cyclosporine, azathioprine, mizoribine, and FK506; other drugs noted are mitotane, visadine, halonitrosoureas, anthrocyclines, and ellipticine. Examples of diagnostic agents are contrast agents for ultrasound, radioactives, and magnetic resonance. Examples of nutritional agents include amino acids, sugars, proteins, **carbohydrates**, fat-soluble vitamins (A, D, E, K), and fats.

ADVANTAGE - Disadvantages of oral administration, including insolubility with low bioavailability, are avoided; also encapsulation protects the drug from liver ''first pass'' effects. Surfactants, as used in Cremophor and other prior art dispersants, can have allergic or even toxic side effects, e.g., myelosuppressive, if used in considerable quantities, as required for taxane type antineoplastics, limiting or preventing continuous administration. Many drugs do associate naturally with serum proteins as carriers in the body, particularly serum albumin. The present method avoids surfactants, but allows solutions containing, e.g., more than 1 mg/ml of taxol, resulting in effective total infusion volumes of less than 300 ml. This improves patient compliance; in addition, ability for continuous dosing without breaks minimises hospital stay. When the carrier is biodegradable, as with proteins, no effects are felt from the system.

Dwg.0/2

FS CPI
FA AB; DCN
MC CPI: B04-C03; B04-N04; B06-A03; B12-M10A; B12-M11E; B14-H01

L102 ANSWER 30 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1998-232413 [21] WPIX
DNC C1998-072599
TI Sustained release formulations containing collagen and glycosaminoglycan - e.g. chondroitin sulphate, hyaluronic acid, heparin, heparan sulphate, dermatan sulphate or keratan sulphate.
DC B04
IN KOSEKI, N; SANO, A
PA (KOKE) KOKEN KK; (SUMU) SUMITOMO PHARM CO LTD; (SUMU) SUMITOMO SEIYAKU KK
CYC 24
PI EP 838219 A1 19980429 (199821)* EN 15p A61K009-20
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
AU 9739907 A 19980423 (199828) A61K047-42
CA 2217134 A 19980409 (199835) A61K047-36
JP 10167987 A 19980623 (199835) 13p A61K047-36
NZ 328898 A 19990225 (199914) A61K009-22
KR 98032708 A 19980725 (199932) A61K009-08
US 5922356 A 19990713 (199934) A61K009-14 <--
AU 727049 B 20001130 (200101) A61K047-42
ADT EP 838219 A1 EP 1997-117479 19971009; AU 9739907 A AU 1997-39907 19971006; CA 2217134 A CA 1997-2217134 19970930; JP 10167987 A JP 1997-293472 19971009; NZ 328898 A NZ 1997-328898 19971003; KR 98032708 A KR 1997-51892 19971009; US 5922356 A US 1997-947463 19971009; AU 727049 B AU 1997-39907 19971006
FDT AU 727049 B Previous Publ. AU 9739907
PRAI JP 1996-268801 19961009
IC ICM A61K009-08; **A61K009-14**; A61K009-20; A61K009-22; A61K047-36; A61K047-42

ICS A61K009-52; A61K031-70; A61K038-17; A61K047-26
ICA A61K038-00; A61K038-27; A61K038-43; A61K038-46; A61K038-55; A61K039-395
AB EP 838219 A UPAB: 19980528
A sustained release formulation contains the active ingredient, collagen as a drug carrier and glycosaminoglycan as an additive.
The glycosaminoglycan is preferably chondroitin sulphate, hyaluronic acid, heparin, heparan sulphate, dermatan sulphate or keratan sulphate (especially chondroitin-6-sulphate or heparin).
USE - The therapeutically active ingredient may be selected from a protein, peptide, glycoprotein, **polysaccharide** or a gene (claimed) e.g. interferon, interleukin, colony-stimulating factor, macrophage-activating factor, insulin, growth hormone or an opioid. Administration may be **parenteral**, topical or systemic.
ADVANTAGE - The compositions provide formulations which allow prolonged and sustained release of a drug.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-B04A1; B04-B04A6; B04-C01G; B04-C02; B12-M10A

L102 ANSWER 31 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1998-232412 [21] WPIX
DNC C1998-072598
TI Controlled release compositions for oral administration of nifedipine - comprising coprecipitate of nifedipine and poly-vinyl-pyrrolidone, hydrophile derivative of cellulose and carboxy-polymethylene and **lactose**.
DC A96 B03
IN VALDUCCI, R
PA (VALP-N) VALPHARMA SA; (VALD-I) VALDUCCI R
CYC 30
PI EP 838218 A1 19980429 (199821)* EN 16p A61K009-14 <--
R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT RO SE SI

AU 9737567	A	19980402	(199823)		A61K009-52
NZ 328783	A	19980226	(199823)		A61K031-44
ZA 9708099	A	19980624	(199831)	25p	A61K000-00
JP 10152440	A	19980609	(199833)	10p	A61K031-455
CA 2216277	A	19980327	(199834)		A61K031-455
US 5871775	A	19990216	(199914)		A61K009-48
BR 9706214	A	19990504	(199924)		A61K009-56
IT 1284604	B	19980521	(200010)		A61K000-00
AU 719075	B	20000504	(200030)		A61K009-52

ADT EP 838218 A1 EP 1997-116153 19970917; AU 9737567 A AU 1997-37567 19970912; NZ 328783 A NZ 1997-328783 19970918; ZA 9708099 A ZA 1997-8099 19970909; JP 10152440 A JP 1997-263279 19970929; CA 2216277 A CA 1997-2216277 19970922; US 5871775 A US 1997-925966 19970909; BR 9706214 A BR 1997-6214 19970926; IT 1284604 B IT 1996-MI1983 19960927; AU 719075 B AU 1997-37567 19970912
FDT AU 719075 B Previous Publ. AU 9737567
PRAI IT 1996-MI1983 19960927
IC ICM A61K000-00; **A61K009-14**; A61K009-48; A61K009-52; A61K009-56; A61K031-44; A61K031-455
ICS A61K009-22; A61K009-28; A61K047-32; A61K047-38
AB EP 838218 A UPAB: 19980528
Controlled release compositions (I) for oral administration containing nifedipine as the active ingredient comprise: (a) **amorphous** coprecipitate of nifedipine and polyvinylpyrrolidone (PVP); (b) hydrophile derivative of cellulose at 0.1-6 wt.% with respect to nifedipine; (c) carboxypolymethylene and **lactose** at 0.1-5 wt.% with respect to nifedipine; and (d) protective or retarding superficial coating.
USE - Nifedipine inhibits the passage of Ca ions in the slow flowing channels which affect the myocardium, vasal smooth musculature and sinoatrial and atrioventricular nodes. It is used to treat hypertension and angina.
ADVANTAGE - (I) are cheaper and simpler to prepare than prior art

compositions.
Dwg.0/4
FS CPI
FA AB; DCN
MC CPI: A03-A04A; A04-D05A; A12-V01; B04-B01C; B04-C02A; B04-C03; B04-C03A; **B04-D01**; B07-D04C; B10-G02; B14-F01D; B14-F02B

L102 ANSWER 32 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1997-527623 [49] WPIX
DNC C1997-168061
TI **Polyol** composition with high concentration of non-hygroscopic **polyol** - obtained by spray-drying or fluidised bed granulation, containing e.g. **mannitol**, **sorbitol** or lactitol, useful in tablet.
DC B07
IN MAUL, K; MOESCHL, G; SCHWARZ, E
PA (MERE) MERCK PATENT GMBH
CYC 30
PI DE 19615418 A1 19971023 (199749)* 12p C07C031-18
WO 9739739 A2 19971030 (199749) DE 31p A61K009-20
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA CN CZ HU JP KR LT LV RU SG SI US
WO 9739739 A3 19971127 (199816) C07C031-18
CZ 9803385 A3 19990113 (199908) A61K009-20
EP 896528 A2 19990217 (199912) DE A61K009-20
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV NL PT SE SI
CN 1216466 A 19990512 (199937) A61K009-20
HU 9903757 A2 20000328 (200025) A61K009-20
JP 2000508668 W 20000711 (200038) 33p A61K009-20
KR 2000005444 A 20000125 (200063) A61K009-20
US 6165511 A 20001226 (200103) A61K009-14 <--
ADT DE 19615418 A1 DE 1996-19615418 19960422; WO 9739739 A2 WO 1997-EP1787 19970410; WO 9739739 A3 WO 1997-EP1787 19970410; CZ 9803385 A3 WO 1997-EP1787 19970410, CZ 1998-3385 19970410; EP 896528 A2 EP 1997-920646 19970410, WO 1997-EP1787 19970410; CN 1216466 A CN 1997-194024 19970410; HU 9903757 A2 WO 1997-EP1787 19970410, HU 1999-3757 19970410; JP 2000508668 W JP 1997-537673 19970410, WO 1997-EP1787 19970410; KR 2000005444 A WO 1997-EP1787 19970410, KR 1998-708212 19981014; US 6165511 A WO 1997-EP1787 19970410, US 1998-171536 19981021
FDT CZ 9803385 A3 Based on WO 9739739; EP 896528 A2 Based on WO 9739739; HU 9903757 A2 Based on WO 9739739; JP 2000508668 W Based on WO 9739739; KR 2000005444 A Based on WO 9739739; US 6165511 A Based on WO 9739739
PRAI DE 1996-19615418 19960422
REP No-SR.Pub; DE 3245170; EP 380219; EP 490768; EP 528604; EP 645096
IC ICM **A61K009-14**; A61K009-20; C07C031-18
ICS A61K031-52; A61K031-60; A61K047-26; B01J002-16; C07C029-94; C07C031-26
AB DE 19615418 A UPAB: 19971211
A composition contains at least two **polyols**, and optionally a binding material, with at least one non-hygroscopic **polyol** comprising more than 80 wt.%. The composition is obtained by co-spray drying or co-fluidised layer granulation.
Also claimed are (1) tablets or compressed materials containing the composition; and (2) preparation of the composition by forming an aqueous solution of the **polyols**; and (a) spraying the solution into an air stream at 120-300 deg. C, where the water evaporates; or (b) introducing into a fluidised bed in an air stream at 40-150 deg. C, where the water evaporates.
USE - The composition is an aid to tablet formation. The tablets contain pharmaceuticals.
Dwg.0/5
FS CPI
FA AB; DCN
MC CPI: B04-C02A2; B10-A07; B10-E04C; B12-M11B

L102 ANSWER 33 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1997-271725 [24] WPIX
CR 1997-246180 [22]
DNC C1997-087323
TI Pharmaceutical composition, in tablet form, for stimulating growth hormone release - comprises N-[1(R)-[(1,2-di hydro-1-methane-sulphonyl-spiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-2-(phenyl-methoxy)ethyl]-2-amino-2-methyl-propan-amide as active agent.
DC A96 B02 C02
IN ASGHARNEJAD, M; DRAPER, J P; DUBOST, D C; KAUFMAN, M J; STOREY, D E; DRAPER, J; DUBOST, D; KAUFMAN, M; STOREY, D
PA (MERI) MERCK & CO INC
CYC 74
PI WO 9715191 A1 19970501 (199724)* EN 92p A01N043-38
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AU AZ BA BB BG BR BY CA CN CU CZ EE GE HU IL IS JP KG KR KZ LC LK LR LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK TJ TM TR TT UA US UZ VN
AU 9675228 A 19970515 (199736) A01N043-38
EP 857020 A1 19980812 (199836) EN A01N043-38
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE
JP 11513989 W 19991130 (200007) 86p C07D471-10
US 6123964 A 20000926 (200051) A61K009-14 <--
ADT WO 9715191 A1 WO 1996-US17196 19961023; AU 9675228 A AU 1996-75228 19961023; EP 857020 A1 EP 1996-937761 19961023, WO 1996-US17196 19961023; JP 11513989 W WO 1996-US17196 19961023, JP 1997-516841 19961023; US 6123964 A Provisional US 1995-5897 19951027, Provisional US 1995-5901 19951027, WO 1996-US17196 19961023, US 1998-66469 19981027
FDT AU 9675228 A Based on WO 9715191; EP 857020 A1 Based on WO 9715191; JP 11513989 W Based on WO 9715191; US 6123964 A Based on WO 9715191
PRAI GB 1996-3834 19960223; US 1995-5897 19951027; US 1995-5901 19951027; GB 1996-3238 19960216; US 1998-66469 19981027
REP US 5578593
IC ICM A01N043-38; **A61K009-14**; C07D471-10
ICS A01N043-42; A61K009-36; A61K031-40; A61K031-445; A61K047-38
AB WO 9715191 A UPAB: 19970612
Pharmaceutical composition comprises:

(a) 0.1-50 weight% of N-[1(R)-[(1,2-dihydro-1methanesulphonylspiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-2(phenylmethoxy)ethyl]-2-amino-2-methyl-propanamide (I), or its salt, as active ingredient,

(b) 0-77 weight% of a binder/diluent selected from hydroxypropyl methylcellulose, hydroxypropyl cellulose, pregelatinised starch and polyvinylpyrrolidone,

(c) 0-77 weight% of a first diluent selected from **lactose**, microcrystalline cellulose, calcium phosphate dibasic, **mannitol**, powdered cellulose and pregelatinised starch,

(d) 0-77 weight% of a second diluent selected from **lactose**, **mannitol**, microcrystalline cellulose, calcium phosphate dibasic, **mannitol**, powdered cellulose and pregelatinised starch,

(e) 0-6 weight% of a disintegrant selected from microcrystalline or croscarmellose sodium,

(f) 0-5 weight% of a lubricant selected from magnesium stearate, calcium stearate and stearic acid.

The sum of components (a)-(f) is at most 100 weight%.

Also claimed are:

(1) the preparation of a tablet containing (I) or its salt, comprising:

(i) forming a powder blend of (I) with a binder/diluent, first and second diluents and a first portion of a disintegrant,

(ii) wet granulating the powder blend with a solution of ethanol/water to form granules,

(iii) drying the granules to remove the ethanol/water,

(iv) adding a second portion of disintegrant,

(v) lubricating the granules and

(vi) compressing the dried granules into tablet form, and

(2) an **amorphous** form of (I) methanesulphonate (Ia).

USE - (I) (which is disclosed in US5536716) is a growth hormone secretagogue which stimulates the release of growth hormone in humans and animals. It may be used to render production of edible meat products and milk more efficient. In humans it may be used to treat physiological/medical conditions characterised by a deficiency in growth hormone secretion and to treat medical conditions which are improved by the anabolic effects of growth hormone. (I) may be used in treatment of, e.g. growth retardation (and associated conditions such as obesity), aging, catabolic side effects of glucocorticoids, osteoporosis, wounds, bone fractures, acute/chronic renal failure or renal insufficiency, Noonan's syndrome, schizophrenia, depression, Alzheimer's disease, pulmonary dysfunction, malabsorption syndromes, gastric ulcers, hyperinsulinaemia, age-related decline of thymic function, immune deficiency, cachexia and protein loss due to chronic illness such as AIDS or cancer, fertility problems and stress-related disorders.
Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: A12-V01; B06-D01; C06-D01; B14-D01; C14-D01

L102 ANSWER 34 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1997-246247 [23] WPIX
DNN N1997-202930 DNC C1997-079994
TI Preparation and use of stabilised biological material by drying without freezing - which contains **carbohydrate** or zwitterion, especially amino acid, and is used for diagnostic and therapeutic purposes, and which possesses increased glass-transition temperature.
DC B04 D16 Q76
IN MATTERN, M; WINTER, G
PA (BOEF) BOEHRINGER MANNHEIM GMBH; (HOFF) ROCHE DIAGNOSTICS GMBH
CYC 75
PI DE 19539574 A1 19970430 (199723)* 32p F26B005-04
WO 9715288 A2 19970501 (199723) DE 57p A61K009-14 <--
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
AU 9672984 A 19970515 (199736) A61K009-14 <--
WO 9715288 A3 19970529 (199737) F26B005-04
ZA 9608930 A 19980624 (199831) 72p F26B000-00
NO 9801868 A 19980625 (199835) A61K009-14 <--
EP 857060 A2 19980812 (199836) DE A61K009-14 <--
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE SI
CZ 9801179 A3 19981111 (199851) A61K009-14 <--
SK 9800509 A3 19981202 (199907) A61K009-14 <--
CN 1205628 A 19990120 (199922) A61K009-14 <--
BR 9611265 A 19990504 (199924) A61K009-14 <--
HU 9901314 A2 19990728 (199936) A61K009-14 <--
AU 712489 B 19991111 (200004) A61K009-14 <--
JP 11513700 W 19991124 (200006) 62p A61K047-18
MX 9803264 A1 19980901 (200017) A61K009-14 <--
NZ 320276 A 19991129 (200031) A61K047-18
KR 99067082 A 19990816 (200045) A61K009-14 <--
TW 387988 A 20000421 (200061) F26B005-04
ADT DE 19539574 A1 DE 1995-19539574 19951025; WO 9715288 A2 WO 1996-EP4627 19961024; AU 9672984 A AU 1996-72984 19961024; WO 9715288 A3 WO 1996-EP4627 19961024; ZA 9608930 A ZA 1996-8930 19961024; NO 9801868 A WO 1996-EP4627 19961024, NO 1998-1868 19980424; EP 857060 A2 EP 1996-934811 19961024, WO 1996-EP4627 19961024; CZ 9801179 A3 WO 1996-EP4627 19961024, CZ 1998-1179 19961024; SK 9800509 A3 WO 1996-EP4627 19961024, SK 1998-509 19961024; CN 1205628 A CN 1996-199329 19961024; BR 9611265 A BR 1996-11265 19961024, WO 1996-EP4627 19961024; HU 9901314 A2 WO 1996-EP4627 19961024, HU 1999-1314 19961024; AU 712489 B AU 1996-72984 19961024; JP 11513700 W WO 1996-EP4627 19961024, JP 1997-516286 19961024; MX 9803264 A1 MX 1998-3264 19980424; NZ 320276 A NZ 1996-320276 19961024, WO 1996-EP4627

19961024; KR 99067082 A WO 1996-EP4627 19961024, KR 1998-703022 19980425; TW 387988 A TW 1996-112857 19961021
FDT AU 9672984 A Based on WO 9715288; EP 857060 A2 Based on WO 9715288; CZ 9801179 A3 Based on WO 9715288; BR 9611265 A Based on WO 9715288; HU 9901314 A2 Based on WO 9715288; AU 712489 B Previous Publ. AU 9672984, Based on WO 9715288; JP 11513700 W Based on WO 9715288; KR 99067082 A Based on WO 9715288
PRAI DE 1995-19539574 19951025
REP DE 4242863; EP 306824; EP 325112; EP 444692; EP 547422; WO 9012029; No-SR.Pub
IC ICM **A61K009-14**; A61K047-18; F26B000-00; F26B005-04
ICS A61K009-16; A61K009-19; A61K031-195; A61K031-70; A61K038-43; A61K047-26; F26B019-00
AB DE 19539574 A UPAB: 19990424
Composition of dry, partially-**amorphous**, biological (especially products containing therapeutically-active material) substances which contain at least:

(i) a **carbohydrate** or zwitterion with polar residues or its derivative, and

(ii) a zwitterion with apolar residues or its derivative. The composition is obtained by drying a solution of the product at a temperature above the freezing point of the solution.

Also claimed is that the glass-transition temperature of the mixture is raised (by at least 10 K), by addition of a substance (ii), compared to substances of type (i) without additives.

USE - The composition is used for diagnostic and therapeutic purposes (claimed).

ADVANTAGE - The addition of the composition avoids the damage to biological materials which normally occurs on freezing.

Dwg.1/3
FS CPI GMPI
FA AB; GI; DCN
MC CPI: B04-C01; B04-E01; B04-F01; B04-F11; B04-G01; B04-L01; B04-L02; B04-N04; B04-N05; B04-N06; B06-D01; B10-B02D; B10-B02E; B10-B02J; B12-M06; D05-H

L102 ANSWER 35 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1997-099994 [09] WPIX
DNC C1997-031954
TI New adjuvant compsns. and **vaccines** - comprising covalently linked **polysaccharide**-phospholipid conjugate to enhance immune responses.
DC B04 B07 C03 C07 D16
IN PARIKH, I
PA (RETR-N) RES TRIANGLE PHARM; (RETR-N) RES TRIANGLE PHARM LTD
CYC 23
PI WO 9701330 A1 19970116 (199709)* EN 45p A61K009-14 <--
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP KR
AU 9664007 A 19970130 (199720) A61K009-14 <--
EP 857059 A1 19980812 (199836) EN A61K009-14 <--
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 5785975 A 19980728 (199837) A61K045-00
KR 99028383 A 19990415 (200027) A61K009-14 <--
ADT WO 9701330 A1 WO 1996-US11051 19960626; AU 9664007 A AU 1996-64007 19960626; EP 857059 A1 EP 1996-923519 19960626, WO 1996-US11051 19960626; US 5785975 A US 1995-494969 19950626; KR 99028383 A WO 1996-US11051 19960626, KR 1997-709699 19971224
FDT AU 9664007 A Based on WO 9701330; EP 857059 A1 Based on WO 9701330; KR 99028383 A Based on WO 9701330
PRAI US 1995-494969 19950626
REP 3.Jnl.Ref; US 4981684; US 5032401; US 5057503; US 5189028; US 5204098
IC ICM **A61K009-14**; A61K045-00
ICS A01N043-04; A01N057-00; A61K031-675; A61K031-715; A61K045-05; A61K047-00
AB WO 9701330 A UPAB: 19980701

Adjuvant useful for administration to a host animal to stimulate immune response comprises a **polysaccharide** (PS)-phospholipid (PL) conjugate in which the conjugate components are linked by a covalent bond.

Also claimed are:

(1) a therapeutic compsn. comprising an antigen or **vaccine** and a PS-PL conjugate in which the conjugate components are linked by a covalent bond;

(2) a method of inducing a immunological response in an animal, embryo or ovum, comprising administering an adjuvant comprising a PS-PL conjugate in which the conjugate components are linked by a covalent bond, to produce an antibody response in the animal, embryo or ovum;

(3) a method of inducing an immunological response in an animal, embryo or ovum, comprising administering a **vaccine** formulation including at least 1 antigen and an adjuvant comprising at least 1 PS-PL conjugate in which the conjugate components are linked by a covalent bond, to produce an antibody response in the animal, embryo, or ovum, and

(4) a method of synthesising an adjuvant from an immuno-stimulating effective PS, comprising covalently conjugating the PS with a PL to form a PS-PL conjugate.

USE - The therapeutic compsns. can be used for disease states and conditions such as smallpox, yellow fever, distemper, cholera, fowl pox, scarlet fever, diphtheria, tetanus, whooping cough, influenza, rabies, mumps, measles, foot and mouth disease, poliomyelitis or tumours. The **vaccine** is administered via subcutaneous **injection**, intravenous **injection**, oral, nasal, ophthalmic, transdermal, intramuscular, intradermal, intraperitoneal, intravaginal, pulmonary, rectal admin. and esp. **parenteral** admin. (all claimed).

ADVANTAGE - The conjugates act as adjuvants which increase the titre, duration, isotype and avidity of the antibody produced in a host animal, and have low toxicity and good effectiveness and safety characteristics in the host animal when compared to Freund's adjuvant.

Dwg.0/2

FS CPI
FA AB; DCN
MC CPI: B04-B01B; C04-B01B; B04-B04C; C04-B04C; B04-C02; C04-C02; B05-B01P; C05-B01P; B14-S11; C14-S11; D05-H07

L102 ANSWER 36 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1997-042654 [04] WPIX
DNC C1997-013437
TI Stabilised solid state dispersions of misoprostol - using **amorphous** or semi-crystalline excipient, inhibit gastric acid secretion and protect mucosa.
DC A96 B05
IN KARARLI, T T; OTTO, D; PENZOTTI, S C; TRUELOVE, J E
PA (SEAR) SEARLE & CO G D
CYC 72
PI WO 9638153 A1 19961205 (199704)* EN 31p A61K031-557
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
AU 9657941 A 19961218 (199714) A61K031-557
ZA 9604482 A 19970827 (199740) 30p A61K000-00
EP 828495 A1 19980318 (199815) EN A61K031-557
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE
JP 11506100 W 19990602 (199932) 27p A61K031-557
US 5935939 A 19990810 (199938) A61K031-70
ADT WO 9638153 A1 WO 1996-US6962 19960522; AU 9657941 A AU 1996-57941 19960522; ZA 9604482 A ZA 1996-4482 19960531; EP 828495 A1 EP 1996-914641 19960522, WO 1996-US6962 19960522; JP 11506100 W JP 1996-536512 19960522, WO 1996-US6962 19960522; US 5935939 A Cont of US 1995-457914 19950601, US 1996-709708 19960909
FDT AU 9657941 A Based on WO 9638153; EP 828495 A1 Based on WO 9638153; JP 11506100 W Based on WO 9638153

PRAI US 1995-457914 19950601; US 1996-709708 19960909
REP 2.Jnl.Ref; US 4301146
IC ICM A61K000-00; A61K031-557; A61K031-70
ICS **A61K009-14**; A61K047-30; A61K047-36; C07C000-00
AB WO 9638153 A UPAB: 19970122
Stable, solid state, **amorphous** dispersion (I) of misoprostol in either (i) an **amorphous** excipient selected from hydroxypropyl-, methyl-, ethyl-, hydroxyethyl-, or carboxymethyl-cellulose, cellulose acetate-phthalate or -butyrate, polyvinyl alcohol, polyethylene glycol, polypropylene, **dextrans**, dextrins, starch, hydroxypropyl-beta-cyclodextrin, chitosan, co-(lactic/glycolic) polymers, poly(orthoester), poly(anhydrate), polyvinyl chloride, polyvinyl acetate, ethylenevinyl acetate, lectins, carbopols, silicon elastomers, polyacrylic polymers and maltodextrin; or (ii) an **amorphous** or semicrystalline excipient selected from mono-, di- and tri-**saccharides**; is new.
USE - Misoprostol, a prostaglandin, inhibits gastric acid secretion and is therefore useful in preventing gastric ulcers.
ADVANTAGE - Prostaglandins generally, including misoprostol, are relatively unstable, partic. in presence of small amts. of acid, base, or water, or at higher temps., e.g., at 55deg.C, 75% of misoprostol is degraded in 4 weeks. Crystalline media also provide poor stability, but using the **amorphous** excipients, potency is better retained, e.g. about 80% after about 8 weeks at 55deg.C.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: A12-V01; B04-C02A2; B04-C02A3; B04-C02B; B04-C02C; B04-C03; **B04-D01**; B04-H03; B04-N04; B07-A02B; B10-A07; B14-E07; B14-E08

L102 ANSWER 37 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1996-413368 [42] WPIX
DNC C1996-130316
TI Stable compsn. contg. trans-glutaminase, esp. factor XIII, and amino acid or sugar stabiliser - opt. also surfactant and reducing agent, dissolves readily to form clear soln. when freeze dried and reconstituted.
DC B04 D16
IN KARGES, H; METZNER, H
PA (AVET) AVENTIS BEHRING GMBH; (BEHW) BEHRINGWERKE AG
CYC 23
PI DE 19508192 A1 19960912 (199642)* 11p C12N009-96
EP 733702 A1 19960925 (199643) DE 16p C12N009-10
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE
AU 9647915 A 19960919 (199645) C12N009-96
NO 9600813 A 19960910 (199646) A61K038-36
JP 08245418 A 19960924 (199648) 13p A61K038-45
CA 2171266 A 19960910 (199702) C12N009-96
NZ 286046 A 19970922 (199745) A61K038-43
CN 1137564 A 19961211 (199805) C12N009-96
AU 2000035419 A 20000824 (200045)# C12N009-10
US 6204036 B1 20010320 (200118) C12N009-96
ADT DE 19508192 A1 DE 1995-19508192 19950309; EP 733702 A1 EP 1996-101959 19960210; AU 9647915 A AU 1996-47915 19960306; NO 9600813 A NO 1996-813 19960228; JP 08245418 A JP 1996-51439 19960308; CA 2171266 A CA 1996-2171266 19960307; NZ 286046 A NZ 1996-286046 19960222; CN 1137564 A CN 1996-102737 19960308; AU 2000035419 A Div ex AU 1996-47915 19960306, AU 2000-35419 20000519; US 6204036 B1 Cont of US 1996-614934 19960311, US 1997-999702 19971222
PRAI DE 1995-19508192 19950309; AU 2000-35419 20000519
REP EP 18561; EP 37078; EP 637451; WO 9200767; WO 9315234
IC ICM A61K038-36; A61K038-43; A61K038-45; C12N009-10; C12N009-96
ICS A61K009-08; **A61K009-14**; A61K009-18; A61K009-19; A61K047-10; A61K047-16; A61P007-02; A61P007-04; C07K014-435; C07K014-78; C12Q001-52
AB DE 19508192 A UPAB: 19961021
Stable compsn. contg. a transglutaminase (I) which is readily soluble

without turbidity after freeze drying comprises: purified (I) and as stabiliser D- and/or L-amino acids (or their salts, derivs., homologues, dimers, oligomers or mixt.), and/or **sugar** or **sugar alcohol**, opt. together with surfactants and/or reducing agents, excluding glycines and arginine.

USE - Specifically (I) is factor XIII (or active fragments, derivs. and muteins) and the compsn. is used in replacement therapy of blood disorders. The compsn. is administered topically or **parenterally**.

ADVANTAGE - The compsn. is storage stable at 2-8 deg.C or higher. The use of human serum albumin is avoided and thus there is no risks of immunogenicity and contamination with virus.

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B04-C02X; B04-C03A; **B04-D01**; B04-H19; B04-L04; B05-A01B; B07-A02B; B07-D09; B10-A07; B10-B01B; B10-B02D; B10-B02J; B10-E03; B10-E04D; B14-F11; D05-H

L102 ANSWER 38 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1996-353786 [35] WPIX
CR 1991-023425 [04]; 1992-042911 [06]; 1997-332008 [30]; 1999-189594 [16]
DNC C1996-111436
TI Microparticle comprising octreotide in form of free base, salt or complex - is distributed in biocompatible, biodegradable copoly(lactife-glycollide) **polyol** ester microparticle matrix, and gives good bio-availability.
DC A96 B04 B07
IN BODMER, D; FONG, J W; KISSEL, T; MAULDING, H V; NAGELE, O; PEARSON, J E
PA (SANO) SANDOZ LTD
CYC 1
PI US 5538739 A 19960723 (199635)* 10p A61K009-14 <--
ADT US 5538739 A CIP of US 1989-377023 19890707, CIP of US 1989-411347 19890922, US 1991-643880 19910118
PRAI US 1991-643880 19910118; US 1989-377023 19890707; US 1989-411347 19890922
IC ICM **A61K009-14**
AB US 5538739 A UPAB: 19990424
A microparticle having a dia. 1-250 mu m comprises 0.2-20 wt.% octreotide, in the form of free base, salt or complex, distributed throughout a biodegradable, biocompatible, polymeric matrix of a 40/60 to 60/40 copoly-(lactide/glycollide) (CPLG) ester of a **polyol**. The **polyol** is either a 3-6C chain contg. alcohol having 3-6 OH gps. or a mono- or di-**saccharide**, all contg. at least 3 CPLG chains.

USE - Octreotide is an analogue of somatostatin and has similar effects. The compsn. is used for long term sustained release therapy of disorders associated with excess GH secretion by the pituitary. These include acromegaly, peptic ulcer, enterocutaneous or pancreaticocutaneous fistula, irritable bowel or dumping syndrome, watery diarrhoea, acute pancreatitis, gastroenteropathic endocrine tumours (vipomas, GRFomas, glucagonomas, insulinomas, gastrinomas and carcinoid tumours), or gastrointestinal bleeding, breast cancer and diabetic complications. Drug release from 1-2 weeks to about 2 months can be obtd.

ADVANTAGE - The compsn. provides good bioavailability of the drug, with higher blood levels and satisfactory release profile, higher and more consistent respectively than prior art compsns. after **parenteral** admin.

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: A05-E02; A12-V01; A12-W05; B04-C03D; B04-J04; B04-J05; B04-J10; B12-M10A; B14-E02; B14-E08; B14-H01; B14-N13; B14-S04

L102 ANSWER 39 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1996-129103 [13] WPIX
DNC C1996-040171

TI Solid dose delivery system - comprises glassy vehicle e.g. stabilising **poly ol** and guest substance e.g. pharmaceutical, esp. useful for **penetrating** epidermis.

DC B07

IN BLAIR, J A; COLACO, C; DUFFY, J A; JERROW, M A Z; KAMPINGA, J; ROSER, B J; WARDELL, J L; DUFFY, J; JERROW, M; JAAP, K

PA (QUAD-N) QUADRANT HOLDINGS CAMBRIDGE LTD; (QUAD-N) QUADRANT HOLDING CAMBRIDGE LTD

CYC 65

PI WO 9603978 A1 19960215 (199613)* EN 102p A61K009-16
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG US UZ VN

AU 9531851	A	19960304	(199623)		A61K009-16
NZ 290896	A	19970424	(199723)		A61K009-16
EP 773781	A1	19970521	(199725)	EN	A61K009-16
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
FI 9700867	A	19970408	(199727)		A61K000-00
NO 9701688	A	19970411	(199728)		A61K047-26
CZ 9700476	A3	19970813	(199739)		A61K009-16
SK 9700277	A3	19970806	(199740)		A61K009-16
AU 688557	B	19980312	(199822)		A61K009-16
JP 10503769	W	19980407	(199824)	95p	A61K047-30
HU 77777	T	19980828	(199844)		A61K009-16
AU 9871864	A	19980820	(199845)		A61K031-71
CN 1204959	A	19990113	(199921)		A61K009-16
AU 707605	B	19990715	(199939)		A61K009-16
MX 9701394	A1	19980301	(200002)		A61K009-16
BR 1100784	A3	19991019	(200013)		A61K031-70

ADT WO 9603978 A1 WO 1995-GB1861 19950804; AU 9531851 A AU 1995-31851 19950804; NZ 290896 A NZ 1995-290896 19950804, WO 1995-GB1861 19950804; EP 773781 A1 EP 1995-927856 19950804, WO 1995-GB1861 19950804; FI 9700867 A WO 1995-GB1861 19950804, FI 1997-867 19970228; NO 9701688 A WO 1995-GB1861 19950804, NO 1997-1688 19970411; CZ 9700476 A3 WO 1995-GB1861 19950804, CZ 1997-476 19950804; SK 9700277 A3 WO 1995-GB1861 19950804, SK 1997-277 19950804; AU 688557 B AU 1995-31851 19950804; JP 10503769 W WO 1995-GB1861 19950804, JP 1996-506345 19950804; HU 77777 T WO 1995-GB1861 19950804, HU 1998-694 19950804; AU 9871864 A Div ex AU 1995-31851 19950804, AU 1998-71864 19980612; CN 1204959 A CN 1995-195496 19950804; AU 707605 B Div ex AU 1995-31851 19950804, AU 1998-71864 19980612; MX 9701394 A1 MX 1997-1394 19970224; BR 1100784 A3 BR 1997-1100784 19970512

FDT AU 9531851 A Based on WO 9603978; NZ 290896 A Based on WO 9603978; EP 773781 A1 Based on WO 9603978; CZ 9700476 A3 Based on WO 9603978; AU 688557 B Previous Publ. AU 9531851, Based on WO 9603978; JP 10503769 W Based on WO 9603978; HU 77777 T Based on WO 9603978; AU 707605 B Div ex AU 688557, Previous Publ. AU 9871864

PRAI US 1994-349029 19941202; GB 1994-15810 19940804

REP 1.Jnl.Ref; DE 1080265; WO 8808298; WO 9011756; WO 9118091; WO 9310758; WO 9422423

IC ICM A61K000-00; A61K009-16; A61K031-70; A61K031-71; A61K047-26; A61K047-30
ICS A61K009-107; **A61K009-14**; A61K009-22; A61K031-715; A61K031-73; A61K031-735; A61K038-22; A61K039-295; A61K039-395

AB WO 9603978 A UPAB: 19960329
A compsn. comprises a solid dose delivery system comprising a glassy vehicle and an effective amt. of at least one guest substance. The vehicle is one in which the guest substance can be dried and stored without losses in activity.

Also claimed is the mfr. of a vitreous solid dose delivery system comprising (a) processing at least one first component capable of forming a glassy vehicle and at least one second component to be a guest substance to form a mixt., and (b) forming the mixt. into a desired shape.

Also claimed is a method of obtaining an aq. suspension of a guest substance, pref. soluble in organic solvents comprising (a) dissolving the guest substance soluble in organic solvents, and **trehalose**, in

an aq./organic solvent mix, (b) drying the mixt. to obtain a solid soln. or suspension of the guest substance in a **trehalose** glass and (c) dissolving the solid soln. in an aq. solvent.

USE - The delivery systems are suitable for delivery of bioactive material to subcutaneous and intradermal, intramuscular and intravenous tissue, the delivery system being sized and shaped for penetrating the epidermis.

ADVANTAGE - The guest substance has increased stability in the presence of elevated temps. or organic solvents.

Dwg.0/18

FS CPI
FA AB; DCN
MC CPI: B01-C04; B01-C05; B01-C06; B04-A07E; B04-B03B; B04-B03C; B04-C02; B04-F01; B04-F10; B04-F11; B04-G21; B04-H01; B04-H02; B04-H05; B04-L01; B04-N04; B07-A02A; B07-A02B; B10-A07; B14-A01; B14-A02; B14-C01; B14-C03; B14-E12; B14-F01A; B14-F02B; B14-F02D; B14-F04; B14-G02; B14-H01B; B14-J01A1; B14-J01A3; B14-J01B3; B14-J01B4; B14-J02B1; B14-L09; B14-M01C; B14-N08

L102 ANSWER 40 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1996-010669 [01] WPIX
DNC C1996-003324
TI Microparticle delivery system contg. organo metallic silicone polymer - use esp. for immunogens, as for **vaccination**, diagnosis, and treatment of bacterial and viral infections, and can be given mucosally..
DC A96 B07
IN BROOK, M A; HERITAGE, P L; JIANG, J; LOOMES, L M; MCDERMOTT, M R; UNDERDOWN, B J
PA (UYMC-N) UNIV MCMASTER
CYC 62
PI WO 9531187 A1 19951123 (199601)* EN 56p A61K009-58
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SI SK TJ TT UA US UZ VN
AU 9524419 A 19951205 (199620) A61K009-58
US 5571531 A 19961105 (199650) 21p A61K009-56
EP 762875 A1 19970319 (199716) EN A61K009-58
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
EP 762875 B1 20001220 (200105) EN A61K009-58
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 69519670 E 20010125 (200112) A61K009-58
ES 2153034 T3 20010216 (200114) A61K009-58
ADT WO 9531187 A1 WO 1995-CA294 19950518; AU 9524419 A AU 1995-24419 19950518; US 5571531 A US 1994-245646 19940518; EP 762875 A1 EP 1995-918482 19950518, WO 1995-CA294 19950518; EP 762875 B1 EP 1995-918482 19950518, WO 1995-CA294 19950518; DE 69519670 E DE 1995-619670 19950518, EP 1995-918482 19950518, WO 1995-CA294 19950518; ES 2153034 T3 EP 1995-918482 19950518
FDT AU 9524419 A Based on WO 9531187; EP 762875 A1 Based on WO 9531187; EP 762875 B1 Based on WO 9531187; DE 69519670 E Based on EP 762875, Based on WO 9531187; ES 2153034 T3 Based on EP 762875
PRAI US 1994-245646 19940518
REP EP 256933; EP 271979; US 5075109
IC ICM A61K009-56; A61K009-58
ICS A01N025-34; **A61K009-14**; A61K009-50
AB WO 9531187 A UPAB: 19960108
Particulate carrier comprising: (a) a solid core comprising a **polysaccharide** and a proteinaceous material; and (b) an organometallic polymer bound to the core; is new.

USE - The carrier is used, esp. in microparticle form, for delivery of bioactive materials to humans and other animals. These are partic. immunogenic materials, including proteins, peptides, antigens, antibodies, bacteria and viruses and their lysates, haptens, **carbohydrates**, nucleic acids, lipids and glycolipids, also other pharmacologically active materials, or their combinations, derivs. and mixts.. Examples of proteins are human or human serum albumin; of viruses are influenza, measles,

mumps, HIV, polio, rubella, herpes simplex 1 and 2, hepatitis A, B, C, yellow fever, smallpox, rabies, **vaccinia**, rota-, rheo- and rhino-virus, Echo, Coxsackie, papilloma, and adenovirus. Lists of bacteria, and yeasts, are also included.

ADVANTAGE - The proteinaceous material, which may also be the bioactive material, can be incorporated into the carrier at temps. which do not denature or otherwise deactivate it. The organometallic coating provides protection and improved safety in manufacture, also improving ease of storage, without affecting biocompatibility. The protective coating also allows mucosal, e.g. oral and nasal, as well as normal **parenteral** delivery, and improved immunogenicity, partic. for antigens not normally giving a good response.

Dwg.1/16

FS CPI
FA AB; GI; DCN
MC CPI: A03-A01; A03-C01; A06-A00E3; A12-V01; A12-V03; B04-B04C1; B04-B04C2; B04-C03D; B04-F10; B04-F11; B12-K04A; B12-M02F; B12-M11; B14-A01; B14-A02; B14-C02; B14-N02; B14-S11
ABEQ US 5571531 A UPAB: 19961211

A particulate carrier, which comprises:

a solid matrix comprising a **polysaccharide** and a proteinaceous material, and a functionalised silicone polymer bonded to the matrix.

Dwg.0/12

L102 ANSWER 41 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1995-392779 [50] WPIX
CR 1994-007461 [01]; 1994-341503 [42]; 1995-036072 [05]; 1995-178642 [23]; 1995-392800 [50]; 1996-200699 [20]; 1996-209175 [21]; 1996-230351 [23]; 1996-230352 [23]; 1996-251443 [25]; 1996-342056 [34]; 2000-411184 [34]
DNC C1995-169194
TI Acyl amino acids and peptide(s) as bioactive agent carriers - allow oral delivery of agents normally inactivated in GI tract or not absorbed e.g., growth hormone, heparin, insulin, interferon, antibody.
DC B04 C03
IN LEONE-BAY, A; WANG, N F
PA (EMIS-N) EMISPHERE TECHNOLOGIES INC
CYC 65
PI WO 9528838 A1 19951102 (199550)* EN 53p A01N037-46
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA US UZ VN
AU 9523963 A 19951116 (199608) A01N037-46
EP 758843 A1 19970226 (199714) EN A01N037-46
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
US 5629020 A 19970513 (199725) 30p A61K009-14 <--
JP 09512279 W 19971209 (199808) 55p C07C233-63
MX 9604539 A1 19970901 (199850) A01N037-46
US 5935601 A 19990810 (199938) A61K009-14 <--
US 6180140 B1 20010130 (200108) A61K009-14 <--
ADT WO 9528838 A1 WO 1995-US5112 19950421; AU 9523963 A AU 1995-23963 19950421; EP 758843 A1 EP 1995-917157 19950421, WO 1995-US5112 19950421; US 5629020 A US 1994-231622 19940422; JP 09512279 W JP 1995-527834 19950421, WO 1995-US5112 19950421; MX 9604539 A1 MX 1996-4539 19961002; US 5935601 A Cont of US 1994-231622 19940422, WO 1995-US5112 19950421, US 1996-732404 19961022; US 6180140 B1 Div ex US 1994-231622 19940422, US 1995-460265 19950602
FDT AU 9523963 A Based on WO 9528838; EP 758843 A1 Based on WO 9528838; JP 09512279 W Based on WO 9528838; US 5935601 A Cont of US 5629020, Based on WO 9528838; US 6180140 B1 Div ex US 5629020
PRAI US 1994-231622 19940422; US 1996-732404 19961022; US 1995-460265 19950602
REP US 4757066; US 4873087; US 4925673; US 5066487
IC ICM A01N037-46; **A61K009-14**; C07C233-63
ICS A01N037-20; A61K009-20; A61K009-48; A61K031-35; A61K038-00;

A61K038-11; A61K038-22; A61K038-23; A61K038-27; A61K038-28; A61K039-00; A61K039-395; A61K047-42; C07C229-00; C07C233-50; C07K005-062; C07K005-065; C07K005-068

AB WO 9528838 A UPAB: 20010207

Compsn. comprising (a) biologically active agent(s); and (b) acylated amino acid(s) and/or peptide(s) contg. acylated amino acid gp(s); in which the acyl residue is (A) 4-11C cycloalkanoyl (opt. substd. by 1-7C alkyl or alkoxy, 2-7C alkenyl, OH, phenyl, phenoxy, COOH, 2-5C alkoxycarbonyl, or 3-5C alkenoxycarbonyl); or (B) 3-10C cycloalkyl 1-6C alkanoyl; is new.

USE - The acyl amino acids are used as carriers for delivery of bioactive agents to animals including humans, birds and insects. These carriers are partic. valuable for those agents normally not given orally, due to sensitivity to conditions in the gastrointestinal tract, or hydrophilic agents which may be charged and not absorbed readily from the gut. These agents include peptides, **mucopolysaccharides**, **carbohydrates**, lipids, and pesticides. Partic. examples are human and bovine growth hormone, growth hormone releasing hormone, interferon, interleukin II, insulin, heparin, calcitonin, erythropoietin, atrial natriuretic factor, antigens, monoclonal antibodies, somatostatin, adrenocorticotropin, gonadotrophin releasing hormone, oxytocin, vasopressin, Na cromolyn, vancomycin, and desferrioxamine. These agents can then be given orally, as tablets, capsules, or liqs., although **parenteral** admin. of microspheres is mentioned.

ADVANTAGE - Oral admin. of bioactive agents is more convenient, and the particle size, partic. as microspheres 0.1-10 mu dia., can determine area of release in the GI tract. The acyl amino acid carriers are easily prepd. and inexpensive, and the method in amenable to industrial scale up.

Dwg.1/17

FS CPI

FA AB; GI; DCN

MC CPI: B04-C01; B04-C02; B04-C02E; B04-C03C; B04-J04A; B04-J05A; B04-J05B; B04-J07; B04-J10; B04-N02; B06-A01; B06-H; B07-H; B10-A17; B10-A18; B10-B02H; B10-D03; B12-M11E; B02-V; C02-V; B04-B04C; C04-B04C

ABEQ US 5629020 A UPAB: 19970619

A composition comprising: (A) at least one biologically active agent selected from the group consisting of a peptide, a mucopoly-**saccharide**, a **carbohydrate**, a lipid, a pesticide, or any combination thereof, and (B) (a) at least one acylated amino acid; (b) at least one peptide comprising at least one acylated amino acid; or (c) a combination of (a) and (b); wherein said acylated amino acid is acylated by a C3-C10 cycloalkyl acylating agent.

Dwg.0/17

L102 ANSWER 42 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1995-082823 [12] WPIX

DNC C1995-037268

TI Ubidecarenone microparticle and nanoparticle formulation - provides improved bio-availability and drug carrier system for incorporated active agents, esp. for intravenous admin..

DC A96 B05 B07 C03 C07 D13 D21 P73

IN SIEKMANN, B; WESTESEN, K

PA (WEST-I) WESTESEN K; (SIEK-I) SIEKMANN B; (KNOL) KNOLL AG

CYC 57

PI DE 4327063 A1 19950216 (199512)* 20p C07C050-28

WO 9505164 A1 19950223 (199513) EN 48p A61K009-14 <--

RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE

W: AM AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB GE HU JP KE KG KP KR KZ LK LT LU LV MD MG MN MW NL NO NZ PL PT RO RU SD SE SI SK TJ TT UA US UZ VN

AU 9473926 A 19950314 (199525) A61K009-14 <--

EP 711151 A1 19960515 (199624) EN A61K009-14 <--

R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE

JP 09502963 W 19970325 (199722) 73p A61K009-00

EP 711151 B1 20000503 (200026) EN A61K009-14 <--

R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE

DE 69424288 E 20000608 (200034) A61K009-14 <--

ES 2145146 T3 20000701 (200036) A61K009-14 <--
US 6197349 B1 20010306 (200115) A61K009-50

ADT DE 4327063 A1 DE 1993-4327063 19930812; WO 9505164 A1 WO 1994-SE728 19940809; AU 9473926 A AU 1994-73926 19940809; EP 711151 A1 EP 1994-923855 19940809, WO 1994-SE728 19940809; JP 09502963 W WO 1994-SE728 19940809, JP 1995-506899 19940809; EP 711151 B1 EP 1994-923855 19940809, WO 1994-SE728 19940809; DE 69424288 E DE 1994-624288 19940809, EP 1994-923855 19940809, WO 1994-SE728 19940809; ES 2145146 T3 EP 1994-923855 19940809; US 6197349 B1 Cont of WO 1994-SE728 19940809, Cont of US 1996-591582 19960207, US 1997-968899 19971106

FDT AU 9473926 A Based on WO 9505164; EP 711151 A1 Based on WO 9505164; JP 09502963 W Based on WO 9505164; EP 711151 B1 Based on WO 9505164; DE 69424288 E Based on EP 711151, Based on WO 9505164; ES 2145146 T3 Based on EP 711151

PRAI DE 1993-4327063 19930812

REP 5.Jnl.Ref; DE 3524788; JP 61068412

IC ICM A61K009-00; **A61K009-14**; A61K009-50; C07C050-28
ICS A01N025-12; A01N033-18; A01N043-30; A01N053-08; A01N057-14; A01N057-26; A61K009-12; A61K009-51; A61K031-12; A61K031-19; A61K031-215; A61K031-23; A61K031-56; A61K031-59; A61K047-30; B01F003-00; B01F017-00; B01J013-02; B32B005-16; C07C046-10; C07C050-06

AB DE 4327063 A UPAB: 20010418

Ubidecarenone (coenzyme Q10) particles which have a diameter of 10 nm to 10 mu and which are **amorphous** at room temp. (20 deg. C) are claimed.

Particles are suitably stabilised using one or more opt. hydrogenated phospholipids, (glyco)sphingolipids, cholanic acid salts, sterols, satd. or unsatd. fatty acids and fatty **alcohols** as well as their resp. salts, ethoxylated derivs. and ethers and esters (including those derived from **sugars**), opt. ethoxylated sorbitan esters and ethers, partial fatty acid glycerides, synthetic biocompatible polymers (e.g. block polymers of polyethylene- and polypropylene oxides), amino acids, polypeptides, proteins and peptisators.

USE - Particles are used for the **parenteral**, oral, peroral, rectal, nasal, pulmonal, ocular and topical admin. of ubidecarenone or other active agents in pharmaceutical, dietetic, food, cosmetic and veterinary formulations. The particles may also act as a drug carrier system for active agents which are dissolved, dispersed or solubilised in the particles or adsorbed on their surface. They are esp. suitable for i.v. admin. of agents which are difficultly soluble in water, highly lipophilic and/or have low bioavailability. Such agents include antibiotics, e.g. fosfomycin, antihypertonics, e.g. minoxidil, antiphotonics, e.g. dihydro-ergotamine, antimycotics, e.g. ketoconazole, antiinflammatories, e.g. indomethacin, antivirals, e.g. acyclovir, ACE inhibitors, e.g. captopril, beta-blockers, e.g. propanolol, bronchodilators, e.g. ipratropium bromide, Ca antagonists, e.g. diltiazem, cardiac glycosides, e.g. digitoxin, cephalosporins, e.g. ceftizoxime, cytostatics, e.g. cyclophosphamide, hypnotics and sedatives, e.g. flurazepam, psycho-pharmaceuticals, e.g. oxazepam, steroid hormones, e.g. cortisone, vasodilators, e.g. molsidomine, cerebral vasodilators, e.g. di:hydro-ergotoxin, and fat-soluble vitamins.

ADVANTAGE - Compared with prior art formulations, the particles provide improved ubidecarenone dosage forms, esp. for i.v. admin., which increase its bio-availability and enable its controlled distribution in the body. When used as a drug carrier system, the particles avoid disadvantages of conventional systems such as liposomes and fatty emulsions, e.g. embolism formation following i.v. admin. Further, the particles are also simple, safe and economical to produce.

Dwg.0/10

FS CPI GMPI

FA AB; DCN

MC CPI: A12-V01; B04-L02; B12-M11E; B04-L02; C04-L02; B12-M11E; C12-M11E; C04-L02; C12-M11E; D03-H01T; D08-B; D08-B10

AN 1995-053453 [08] WPIX
DNC C1995-024320
TI **Parenteral** compsn. for controlled drug release - using liq. bio-absorbable lactone polymer as carrier.
DC A23 A96 B07 C07
IN ARNOLD, S C; BEZWADA, R S; SHALABY, S W; WILLIAMS, B L
PA (ETHI) ETHICON INC
CYC 5
PI EP 635272 A1 19950125 (199508)* EN 10p A61K047-34
R: FR GB
CA 2128361 A 19950121 (199516) A61K047-34
JP 07166042 A 19950627 (199534) 8p C08L067-04
US 5631015 A 19970520 (199726) 7p A61F013-00
US 5653992 A 19970805 (199737) 8p A61F002-00
EP 635272 B1 20000315 (200018) EN A61K047-34
R: FR GB
ADT EP 635272 A1 EP 1994-305273 19940719; CA 2128361 A CA 1994-2128361 19940719; JP 07166042 A JP 1994-184117 19940714; US 5631015 A Cont of US 1993-94823 19930720, US 1996-650562 19960520; US 5653992 A Div ex US 1993-94823 19930720, US 1995-429375 19950426; EP 635272 B1 EP 1994-305273 19940719
PRAI US 1993-94823 19930720; US 1996-650562 19960520; US 1995-429375 19950426
REP 01Jnl.Ref; FR 2390962; US 4818542; WO 9005522; WO 903768; WO 9402184
IC ICM A61F002-00; A61F013-00; A61K047-34; C08L067-04
ICS A61K009-00; A61K009-08; **A61K009-14**; A61K031-785; A61K045-00; C08K005-15
AB EP 635272 A UPAB: 19950301
Parenteral compsn. comprising drug(s) and a bioabsorbable lactone polymer, liq. at body temp., from one or more lactone monomers.
Polymers generally should be liq. at 25 deg.C and have inherent viscosity below 0.8 dL/g for ease of **injection**, but above 0.05 dL/g for satisfactory controlled release. The monomers used in the polymer are glycolide, L- or DL-lactide, 1,4-dioxanone, e-caprolactone, 1,5-dioxepan-2-one, and trimethylene carbonate. Bipolymers are e.g. lactide/e-caprolactone, lactide/p-dioxanone, etc.
USE - The compsn. is used for delivery of a wide range of drugs subcutaneous or i.m. not only to humans, but to domestic animals, including dogs, cats, cattle, sheep, and horses. Also used for hormones, immunosuppressives, natural or engineered proteins, glycoproteins, lipoproteins, or **polysaccharides**.
ADVANTAGE - Isotonic solns. provide drug immediately for **injection**, and are not always well suited for some drugs or for prolonged therapy. The copolymer, on contact with body fluids, undergoes gradual degradation, mainly hydrolysis, to release the drug for delivery over of 2-800 hr. Use of a liq. carrier for the drug also avoids the disadvantages of solid implants, e.g., toxic solvent trace residues.
Dwg.0/3
FS CPI
FA AB; DCN
MC CPI: A05-E02; A09-A07; A12-V01; B04-C02; C04-C02; B04-C03; C04-C03; B04-J01; C04-J01; B04-N04; C04-N04; B12-M10A; C12-M10A; C04-C03D
ABEQ US 5631015 A UPAB: 19970626
A liquid **parenteral** composition for **injection** subcutaneously or intramuscularly into animals comprises at least one drug consisting essentially of an admixture; and a bioabsorbable lactone copolymer composed of two lactone monomers selected from L-lactide, 1,4-dioxanone, epsilon-caprolactone, 1,5-dioxepan-2-one and trimethylene carbonate the copolymer being a liquid at body temperature, provided in an amount effective to sustain or extend the release rate of the drug, the inherent viscosity of the copolymer is 0.05-0.8 dL/g as determined in a 0.1 g/dL solution of hexafluoroisopropanol at 25 deg. C and the lactone copolymer contains substantially no unreacted monomer.
Dwg.0/3
ABEQ US 5653992 A UPAB: 19970915
A **parenteral** composition for **injection** subcutaneously

or intramuscularly into animals of at least one drug consisting essentially of an admixture of at least one drug to be delivered in a therapeutically effective amount; and a bioabsorbable lactone terpolymer having three or more lactone monomers that is a liquid at body temperature, provided in an amount effective to sustain or extend the release rate of the drug, wherein the inherent viscosity of the terpolymer is between about 0.05 dL/g and about 0.8 dL/g as determined in a 0.1 g/dL solution of hexafluoroisopropanol at 25 deg. C. and the lactone terpolymer contains substantially no unreacted monomer.
Dwg.0/3

L102 ANSWER 44 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1994-248899 [30] WPIX
DNC C1994-113197
TI Immediate and controlled release **vaccine** preparation - comprises immunogen adsorbed onto aluminium salt adjuvant, used in human and veterinary medicine reducing time and costs.
DC A96 B04 C06 D16
IN COX, J C; JACOBS, I C; MASON, N S; SPARKS, R E
PA (CSLC-N) CSL LTD
CYC 23
PI WO 9415636 A1 19940721 (199430)* EN 37p A61K039-39
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA JP KR NZ US
AU 9458053 A 19940815 (199442) A61K039-39
EP 678035 A1 19951025 (199547) EN A61K039-39
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
AU 667003 B 19960229 (199616) A61K039-39
NZ 259285 A 19960726 (199635) A61K039-39
JP 08505152 W 19960604 (199648) 34p A61K039-39
EP 678035 A4 19970226 (199728) A61K039-39
US 5902565 A 19990511 (199926) A61K051-00
ADT WO 9415636 A1 WO 1993-AU677 19931224; AU 9458053 A AU 1994-58053 19931224; EP 678035 A1 WO 1993-AU677 19931224, EP 1994-903697 19931224; AU 667003 B AU 1994-58053 19931224; NZ 259285 A NZ 1993-259285 19931224, WO 1993-AU677 19931224; JP 08505152 W WO 1993-AU677 19931224, JP 1994-515529 19931224; EP 678035 A4 EP 1994-903697 ; US 5902565 A CIP of US 1993-2485 19930108, CIP of WO 1993-AU677 19931224, WO 1993-AU677 19931224, US 1995-481403 19950710
FDT AU 9458053 A Based on WO 9415636; EP 678035 A1 Based on WO 9415636; AU 667003 B Previous Publ. AU 9458053, Based on WO 9415636; NZ 259285 A Based on WO 9415636; JP 08505152 W Based on WO 9415636; US 5902565 A Based on WO 9415636
PRAI US 1993-2485 19930108; US 1995-481403 19950710
REP AU 8929557; AU 8941876; CH 5645270; US 5242686; 4.Jnl.Ref; WO 9210208; WO 9409898
IC ICM A61K039-39; A61K051-00
ICS **A61K009-14**; A61K009-16; A61K009-50; A61K009-52; A61K009-60; A61K039-05; A61K039-08; A61K039-10; A61K047-48
AB WO 9415636 A UPAB: 19940914
Immediate release **vaccine** prepn. in stable particulate form prepd. by spray drying comprises an immunogen (IM) adsorbed onto an aluminium salt adjuvant (ASA).

Also claimed are: (a) a controlled or delayed release **vaccine** prepn. in stable particulate form, the particles being microspheres prepd. by spray drying, comprising a continuous matrix of biodegradable polymer contg. discrete IM-contg. regions; and (b) a **vaccine** compsn. contg. at least one immediate release **vaccine** prepn. (IRV) and opt. at least one controlled or delayed release **vaccine** prepn. (CRV) and a carrier or diluent.

The ASA is aluminium hydroxide or phosphate and the compsn. further comprises a protein stabiliser pref. a sugar or sugar deriv. esp. a **trehalose, lactose**, dextrose or glucosamine. The particulate form is pref. a free flowing powder.

USE/ADVANTAGE - The **vaccines** are used as human or veterinary **vaccines**. They are formulated as solid pellets or

implants or for **parenteral** admin. The **vaccines** give a full course of **vaccine** in a single dose reducing time, (the animals need only be handled once), cost (a single veterinary visit) and gives guaranteed compliance with recommended dose schedule (no. of doses and time interval between doses; and in human medicine are important in developing countries where repeated access to infants is not possible, and where there is pain and suffering associated with **vaccination**.. Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: A12-V; A12-V01; B04-G01; C04-G01; B05-A01B; C05-A01B; B12-M10; C12-M10; B12-M11D; C12-M11D; B14-S11; C14-S11; C05-A01B; C05-B02A3; C07-A02B; C10-A07; C12-M11E; C12-M11G; C14-S11; D05-H07

L102 ANSWER 45 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1994-234306 [28] WPIX
DNC C1994-106515
TI Controlled release pharmaceutical formulation prodn. - by (electro)mechanical treatment of mixt. of drug and excipient opt. followed by pelletising, for delayed or rapid release.
DC A96 B07 C07
IN MOTTA, G
PA (DIOL-I) DIOLAITI L; (SAIT-N) SAITEC SRL
CYC 33
PI WO 9414421 A2 19940707 (199428)* EN 29p A61K009-20
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU BR CA CZ FI HU JP KR NO NZ PL RO RU SK UA US
AU 9460434 A 19940719 (199439) A61K009-20
WO 9414421 A3 19940818 (199518) A61K009-20
EP 675710 A1 19951011 (199545) EN A61K009-20
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
JP 08504807 W 19960528 (199646) 31p A61K009-00
IT 1260242 B 19960402 (199649) A61K000-00
IT 1263445 B 19960805 (199711) A61K000-00
IT 1268454 B 19970304 (199738) A61K000-00
US 5662935 A 19970902 (199741) 13p A61K009-14 <--
AU 683044 B 19971030 (199751) A61K009-22
EP 675710 B1 19990825 (199939) EN A61K009-20
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 69326163 E 19990930 (199946) A61K009-20
BR 9307736 A 19990831 (200002) A61K009-20
ES 2138070 T3 20000101 (200008) A61K009-20
RU 2128499 C1 19990410 (200024) A61K009-00
ADT WO 9414421 A2 WO 1993-IT136 19931223; AU 9460434 A AU 1994-60434 19931223; WO 9414421 A3 WO 1993-IT136 19931223; EP 675710 A1 WO 1993-IT136 19931223, EP 1994-906994 19931223; JP 08504807 W WO 1993-IT136 19931223, JP 1994-514993 19931223; IT 1260242 B IT 1992-BO455 19921223; IT 1263445 B IT 1993-BO294 19930624; IT 1268454 B IT 1993-BO460 19931112; US 5662935 A WO 1993-IT136 19931223, US 1995-464708 19950623; AU 683044 B AU 1994-60434 19931223; EP 675710 B1 WO 1993-IT136 19931223, EP 1994-906994 19931223; DE 69326163 E DE 1993-626163 19931223, WO 1993-IT136 19931223, EP 1994-906994 19931223; BR 9307736 A BR 1993-7736 19931223, WO 1993-IT136 19931223; ES 2138070 T3 EP 1994-906994 19931223; RU 2128499 C1 WO 1993-IT136 19931223, RU 1995-113481 19931223
FDT AU 9460434 A Based on WO 9414421; EP 675710 A1 Based on WO 9414421; JP 08504807 W Based on WO 9414421; US 5662935 A Based on WO 9414421; AU 683044 B Previous Publ. AU 9460434, Based on WO 9414421; EP 675710 B1 Based on WO 9414421; DE 69326163 E Based on EP 675710, Based on WO 9414421; BR 9307736 A Based on WO 9414421; ES 2138070 T3 Based on EP 675710; RU 2128499 C1 Based on WO 9414421
PRAI IT 1992-BO455 19921223; IT 1993-BO294 19930624; IT 1993-BO460 19931112
REP No-SR.Pub; 5.Jnl.Ref; EP 15381; EP 392608; EP 467743; EP 80341; JP 01009932; JP 03287544; JP 47020327; JP 58172311; JP 60094403; US 3146167; WO 9205774
IC ICM A61K000-00; A61K009-00; **A61K009-14**; A61K009-20; A61K009-22

ICS A01N025-10; A61J003-00; A61J003-10; A61K009-24; A61K009-26; A61K009-52

AB WO 9414421 A UPAB: 19940831

Prepn. of controlled release pharmaceutical formulations comprises: (i) subjecting a mixt. of excipient(s) (I) and active ingredient(s) (II) to mechanical or electromechanical action for a predetermined time (pref. 0.1-20 secs.) and within a wide range of frequencies (pref. between 1 kHz and 2MHz) film; and opt., (ii) pelletising the prod. to give pellets having dia. 2.5mm or less which retain the same controlled release properties. Also claimed are formulations obtd. by step (i) (for oral, topical or **parenteral** admin., pref. of dia. 2-15mm as tablets or matrix or size 4mm to 30cm. as a film, and of thickness 0.1-10mm); and powder or granulate formulations obtd. by steps (i) and (ii) (suitable for direct use or insertion in hard gelatin capsules).

USE/ADVANTAGE - The formulations can be used in the veterinary and agrochemical fields (e.g. for releasing plant hormones, pesticides, fragrances or preservatives), as well as for pharmaceuticals. Typical (II) (not specified in the claims), are vitamins, enzymes, antibiotics (e.g. tetracyclines, penicillins or cephalosporins), diuretics, sedatives, analgesics, bronchodilators, carotenoids, beta-blockers, antiinflammatories, antidepressants, antidiabetic agents, lipids, antihypertensives, vasodilators, vasoconstrictors, hormones, steroids, antihistamines, antitussives, alkaloids, aminoacids, antipyretic, antibacterials, amphetamines, hypnotics, tranquillisers, sympathomimetics, barbiturates, anti-parkinson agents, antimalarials, antispasmodics, topical ophthalmic drugs, interferon, antigens, antibodies, **polysaccharides**, growth factors or anticancer agents. Suitable drugs (II) include dexamethasone, prednisolone, isoproterenol, propranolol, codeine, atropine, hyoscyamine, morphine, streptomycin, Cortisone, isosorbide-5- mononitrate, amobarbital, scopolamine, theophylline, ephedrin, urapidil, ketoprofen, paracetamol, indomethacin, dilhazern, diacerhein, phenylpropanolamine and bile acids. Controlled, delayed or rapid, release of (II) is attained simply by suitable choice of (I). The formulations are easily prepd. without using solvents or prolonged heating. Most drugs currently used in normal or controlled release compsns. can be provided in a wider range of types of formulation.

Dwg.1/6

FS CPI

FA AB; DCN

MC CPI: A12-V01; B04-C02B1; C04-C02B1; B04-C03; C04-C03; B06-D01; C06-D01; B07-A02; C07-A02; B10-A07; C10-A07; B11-C05; C11-C05; B12-M10; C12-M10; B12-M10B; C12-M10B; B12-M11B; C12-M11B; B12-M11C; C12-M11C; B12-M11D; C12-M11D; B12-M11G; C12-M11G

ABEQ US 5662935 A UPAB: 19971013

Preparation controlled release pharmaceutical forms, characterized in that a mixture containing from 30 to 75% by weight of an active ingredient and from 70 to 25% by weight of one or more excipients is compacted by means of mechanically or electromechanically generated ultrasonic energy, said ultrasonic energy having a frequency of up to 2 MHz and being emitted for a period of time of from 1/10 to 20 seconds, to give a tablet, matrix, simple or multilayer film, the tablet or matrix having a diameter of from 2 to 15 mm and the film a size of from 4 mm to 30 cm, the thickness being generally of 0.1 to 10 mm.

Dwg.0/6

L102 ANSWER 46 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1993-196694 [24] WPIX

DNC C1993-087112

TI New sustained release compsn. - comprises **carbohydrate** glass matrix, therapeutic agent e.g. prolactin, somatotropin, growth hormone etc. and hydrophilic agent.

DC A96 B07

IN CUNNINGHAM, J P; RAMAN, S N

PA (PITM) PITMAN MOORE INC

CYC 41

PI WO 9310758 A1 19930610 (199324)* EN 22p A61K009-00

RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA SE
W: AU BB BG BR CA CS FI HU JP KP KR LK MG MN MW NO PL RO RU SD UA

AU 9331251 A 19930628 (199342) A61K009-00
CN 1072861 A 19930609 (199413) A61K037-36
EP 615438 A1 19940921 (199436) EN A61K009-00
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL SE
US 5356635 A 19941018 (199441) 5p A61K009-14 <--
EP 615438 B1 19960724 (199634) EN 9p A61K009-00
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL SE
DE 69212497 E 19960829 (199640) . A61K009-00
ES 2090714 T3 19961016 (199647) A61K009-00
TW 337488 A 19980801 (199849) A61K047-26
CA 2125148 C 19990511 (199937) EN A61K047-44

ADT WO 9310758 A1 WO 1992-US9392 19921102; AU 9331251 A AU 1993-31251 19921102; CN 1072861 A CN 1992-113798 19921204; EP 615438 A1 EP 1992-925051 19921102, WO 1992-US9392 19921102; US 5356635 A Cont of US 1991-802581 19911205, US 1993-91883 19930713; EP 615438 B1 EP 1992-925051 19921102, WO 1992-US9392 19921102; DE 69212497 E DE 1992-612497 19921102, EP 1992-925051 19921102, WO 1992-US9392 19921102; ES 2090714 T3 EP 1992-925051 19921102; TW 337488 A TW 1992-108933 19921109; CA 2125148 C CA 1992-2125148 19921102, WO 1992-US9392 19921102

FDT AU 9331251 A Based on WO 9310758; EP 615438 A1 Based on WO 9310758; EP 615438 B1 Based on WO 9310758; DE 69212497 E Based on EP 615438, Based on WO 9310758; ES 2090714 T3 Based on EP 615438; CA 2125148 C Based on WO 9310758

PRAI US 1991-802581 19911205

REP EP 345628; FR 2383659; US 2918411; WO 8904689; WO 9103237

IC ICM A61K009-00; **A61K009-14**; A61K037-36; A61K047-26; A61K047-44
ICS A61K009-22; A61K037-02; A61K038-18; A61K038-22; A61K038-38; A61K045-00; A61K047-32; A61K047-36

AB WO 9310758 A UPAB: 19931116

New sustained release compsn. comprises **amorphous carbohydrate** glass matrix (I), a therapeutic agent (II), a hydrophobic substance (III) which modifies rate of release of (II) from (I) and opt. an agent (IV) which retards recrystallisation of (I).

(I) and opt. (IV) together comprise 60-90 wt.% of compsn.; total **carbohydrate** content comprises 50-75 wt.% (I) and 15-40 wt.% (II), the remainder being water.

(I) = e.g. a **disaccharide** (e.g. **sucrose** (Ia), **lactose, maltose** or **cellobiose**). (IV) = e.g. polyvinylpyrrolidone (IVa), PVA, polyethylene glycols, maltodextrins, Na lauryl sulphate, oleyl alcohol or stearyl alcohol.

(II) comprises 2-20 wt.% of compsn. and = a polypeptide with mol.wt. 1000-200,000 daltons (e.g. prolactin, serum albumins (bovine, ovine, porcine, avian or human), somatotropins (bovine, ovine, porcine, avian or human) or growth factors (epidermal growth factor, insulin-like growth factor I or II, fibroblast growth factor, transforming growth factor alpha or beta, platelet derived growth factor or nerve growth factor) or any biological fragment or recombinant form of these), vitamin or antibiotic.

(III) = 5-25 wt.% of compsn. and = a wax (e.g. white or yellow beeswax, candelilla wax, carnauba wax, vegetable waxes, castor wax or cetyl esters wax), cholesterol, fatty acid esters or fatty acids.

Compsn. esp. comprises recombinant porcine somatotropin (IIa), (IVa) and beeswax (IIIa) dispersed in an **amorphous sucrose** glass matrix.

USE/ADVANTAGE - The compsn. provides sustained release of (II) and completely degrades in physiological fluids leaving little if any residue. Dissolution is relatively slow and occurs mainly at the surface of the matrix. The compsn. can be prepd. by conventional methods (e.g. extrusion, tabletting).

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: A12-V01; B01-D02; B02-Z; B03-L; B04-B01C; B04-B02D4; B04-B04D2; B04-B04D4; B04-B04J; B04-C01; B04-C03; B07-A02; B10-C04E; B10-G02; B12-M10A

ABEQ US 5356635 A UPAB: 19941206
A new sustained release compsn. for subcutaneous implantation comprises an **amorphous carbohydrate** glass matrix (50-75 % wt.) a biologically active therapeutic agent and a hydrophobic substance (wax) (15-40% wt.) to retard recrystallisation of the **carbohydrate** glass matrix. **Carbohydrates** include **sucrose, lactose, maltose** or celulose. Therapeutics are polypeptides, vitamins or antibiotics, e.g. prolactin, growth hormones, serum albumins, growth factors, and their biologically active fragments and recombinants.
ADVANTAGE - After implantation or oral admin. the compsn. is degraded and absorbed releasing the therapeutic agent gradually over time.
Dwg.0/0
ABEQ EP 615438 B UPAB: 19960829
A sustained release composition comprising an **amorphous carbohydrate** glass matrix, a biologically active therapeutic agent, and a hydrophobic substance which modifies the rate of release of the therapeutic agent from the glass matrix.
Dwg.0/0

L102 ANSWER 47 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1993-134105 [16] WPIX
DNC C1993-059811
TI Stick-like holder for a hardened medicated **matrix** - includes plastic over-cap, comfortable handle and a sealed foil pouch.
DC B07
IN BEST, R J; HADAWAY, M A; KRAMER, D E
PA (ABBO) ABBOTT LAB
CYC 20
PI WO 9306820 A1 19930415 (199316)* EN 21p A61K009-14 <--
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL SE
W: AU CA JP KR
AU 9227633 A 19930503 (199334) A61K009-14 <--
US 5296234 A 19940322 (199411) 7p A61K009-14 <--
JP 07500980 W 19950202 (199514) A61J003-08
US 5490989 A 19960213 (199612) 7p A61K009-14 <--
ADT WO 9306820 A1 WO 1992-US8622 19921009; AU 9227633 A AU 1992-27633 19921009; US 5296234 A US 1991-776543 19911011; JP 07500980 W WO 1992-US8622 19921009, JP 1993-507206 19921009; US 5490989 A Div ex US 1991-776543 19911011, US 1993-175003 19931229
FDT AU 9227633 A Based on WO 9306820; JP 07500980 W Based on WO 9306820; US 5490989 A Div ex US 5296234
PRAI US 1991-776543 19911011; US 1993-175003 19931229
REP US 4671953
IC ICM A61J003-08; **A61K009-14**
ICS A61J001-00; A61J007-00
FS CPI
FA AB; DCN
MC CPI: B07-A02; B07-D05; B11-C06; B12-C08; B12-D01
ABEQ US 5296234 A UPAB: 19940428
A **sucrose**-based matrix contg. a dose of fentanyl citrate is secured to the end of a one-piece moulded plastic handle when has spaced annular rounded grooves for keying to the matrix and has a flat gripping section at the other end to which a pressure-sensitive adhesive label can be attached. There is a transverse flange (32) on the handle to prevent the unit being swallowed.
A tubular moulded plastic overcap closed at one end can fit over the first end to completely enclose the matrix and can pref. snap-fit over the flange. The assembly is pref. sealed in a light-, moisture- and tamper-resistant foil pouch.
USE/ADVANTAGE - Partic. for providing analgesia, sedation and anxiety relief to children or elderly persons. Provides enhanced convenience and safety.
Dwg.0/14
ABEQ US 5490989 A UPAB: 19960322
A protective overcap for a stick holder having a hardened medicated matrix

affixed to a first end portion of the stick holder, said protective overcap comprising a tubular plastic member having a first, closed end and a second, open end opposite said first end, said protective overcap constructed to be fit over the first end portion of the stick holder having a hardened, medicated matrix affixed thereto, and a detent mounted on said protective overcap proximate said second, open end of said protective overcap said detent being constructed to limit movement of the stick holder within said protective overcap and to retain releasably the first end portion of the stick holder within said protective overcap.
Dwg.0/14

L102 ANSWER 48 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1993-001541 [01] WPIX
CR 1999-207105 [18]
DNC C1993-000631
TI Storage of e.g. proteins, nucleotide(s), cells and pharmaceuticals - by mixing material with carrier which forms glassy or rubbery state when dried.
DC A96 B04 D16
IN FRANKS, F; HATLEY, R H M; MATHIAS, S F; HATLEY, R H
PA (PAFR-N) PAFRA LTD; (INHA-N) INHALE THERAPEUTIC SYSTEMS
CYC 11
PI EP 520748 A1 19921230 (199301)* EN 13p B01D001-14
R: DE DK FR GB IT NL SE
AU 9218486 A 19930107 (199308) C12N001-04
CA 2072420 A 19921227 (199311) C12N009-96
JP 05293354 A 19931109 (199349) 10p B01J002-04
AU 659645 B 19950525 (199529) C12N001-04
US 5928469 A 19990727 (199936) B01D001-16
ADT EP 520748 A1 EP 1992-305769 19920624; AU 9218486 A AU 1992-18486 19920623; CA 2072420 A CA 1992-2072420 19920625; JP 05293354 A JP 1992-167431 19920625; AU 659645 B AU 1992-18486 19920623; US 5928469 A Cont of US 1992-902838 19920623, US 1994-241457 19940511
FDT AU 659645 B Previous Publ. AU 9218486
PRAI GB 1992-7839 19920409; GB 1991-13798 19910626
REP DE 1812574; DE 2415159; EP 383569; US 3666496; US 4830858
IC ICM B01D001-14; B01D001-16; B01J002-04; C12N001-04; C12N009-96
ICS A01N001-02; **A61K009-14**; B01D001-18; C07H019-04; C07H021-00; C07K003-00; C07K017-02; C07K017-04; C12N005-00; C12N011-02
AB EP 520748 A UPAB: 19990511
Rendering a material (I) suitable for storage comprises: (a) spraying an aq. mixt. of (I) and a water-soluble or -swellable carrier substance (II), into a hot gas stream, to dry the mixt. to particles contg. (I) and (II) and in which (II) is in a glassy or rubbery state; and (b) sepg. the particles from the gas stream. Storable compsn. produced by the process is also new.

(I) is pref. a protein/peptide (e.g. enzymes, transport protein, immunoglobulin, hormone, blood clotting factor or pharmacologically active peptide or protein) nucleoside, nucleotide, dimucleotide, oligonucleotide, enzyme co-factor or biological cell. The carrier is pref. a polyhydroxy cpd. (e.g. **carbohydrate**), protein, protein hydrolysis prod., or a sugar polymer contg. sugar residues linked through ether bridges to bifunctional gps. other than **carbohydrate**.

(II), When on its own, is able to exist in a glassy **amorphous** state with a glass transition temp. (Tg) above 20 deg.C. (II) Makes up at least 20 wt.% of the particles formed by drying. The compsn. produced by drying has a Tg of at least 20 deg.C esp. at least 50 deg.C..

USE/ADVANTAGE -Used in the biochemical and pharmaceutical fields. Allows for stabilisation of materials for which isolation, purificn. and storage at room temp. is not possible. The materials are easily recovered from the glassy or rubbery compsns. by addn. of water or an aq. soln., or by centrifugation if (I) is not water-solub
Dwg.0/1
FS CPI
FA AB
MC CPI: A12-V01; A12-W11; B04-B02C; B04-B02D; B04-B03; B04-B04A; B04-B04C6;

B04-B04D3; B04-C01; B04-C02; B12-M06; D05-A01A; D05-A01B; D05-H10

L102 ANSWER 49 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1992-358911 [44] WPIX
CR 1995-312557 [41]; 1997-067270 [07]
DNC C1992-159329
TI Storage-stable infusion compsn. for **parenteral** feeding - comprises fat emulsion, **sugar**, aminoacid(s), electrolyte and phosphate of poly hydric **alcohol** or **sugar**, with pH adjusted with organic acid.
DC B07 D13 P33
IN ABE, S; INOUE, T; KODAIRA, H; MURASHIMA, R; NAWA, Y; YOKOYAMA, K
PA (GREC) GREEN CROSS CORP; (YOSH) YOSHITOMI PHARM IND KK; (WELF-N) WELFIDE CORP
CYC 16
PI

EP 510687	A2	19921028 (199244)* EN	33p	A61K009-00	
R: BE CH DE DK ES FR GB IT LI NL SE					
CA 2067062	A	19921027 (199303)		A61K009-107	
JP 05009111	A	19930119 (199311)	6p	A61K009-107	
JP 05031151	A	19930209 (199311)	12p	A61J001-05	
JP 05032540	A	19930209 (199312)	11p	A61K009-107	
JP 05032541	A	19930209 (199312)	6p	A61K009-107	
JP 05065220	A	19930319 (199316)	8p	A61K009-107	
JP 05148149	A	19930615 (199328)	7p	A61K031-66	
JP 05301825	A	19931116 (199350)	4p	A61K037-22	
EP 510687	A3	19930512 (199402)		A61K009-00	
US 5626880	A	19970506 (199724)	15p	A61K009-14	<--
US 5674527	A	19971007 (199746)	16p	A61K009-127	
TW 320563	A	19971121 (199811)		A61K009-08	
JP 2940249	B2	19990825 (199940)	4p	A61K038-00	
JP 2950348	B2	19990920 (199944)	6p	A61K009-107	
US 5972367	A	19991026 (199952)		A61K009-107	
JP 11343229	A	19991214 (200009)	6p	A61K009-107	
JP 3097196	B2	20001010 (200052)	7p	A61K009-107	
KR 244997	B1	20000315 (200122)		A61J001-00	

ADT EP 510687 A2 EP 1992-107054 19920424; CA 2067062 A CA 1992-2067062 19920424; JP 05009111 A JP 1991-222031 19910806; JP 05031151 A JP 1991-209944 19910726; JP 05032540 A JP 1991-209945 19910726; JP 05032541 A JP 1991-209947 19910726; JP 05065220 A JP 1992-27338 19920117; JP 05148149 A JP 1992-131797 19920423; JP 05301825 A JP 1991-222032 19910806; EP 510687 A3 EP 1992-107054 19920424; US 5626880 A Cont of US 1992-873229 19920424, Cont of US 1993-133792 19931008, US 1996-589207 19960122; US 5674527 A Cont of US 1992-873229 19920424, Div ex US 1993-133792 19931008, US 1995-478970 19950607; TW 320563 A TW 1992-103293 19920425; JP 2940249 B2 JP 1991-222032 19910806; JP 2950348 B2 JP 1991-222031 19910806; US 5972367 A Cont of US 1992-873229 19920424, Div ex US 1993-133792 19931008, US 1995-475812 19950607; JP 11343229 A Div ex JP 1991-209947 19910726, JP 1999-102878 19910726; JP 3097196 B2 JP 1991-209947 19910726; KR 244997 B1 Div ex KR 1992-7018 19920425, KR 1999-23090 19990619
FDT JP 2940249 B2 Previous Publ. JP 05301825; JP 2950348 B2 Previous Publ. JP 05009111; JP 3097196 B2 Previous Publ. JP 05032541
PRAI JP 1992-27338 19920117; JP 1991-124866 19910426; JP 1991-124863 19910427; JP 1991-124739 19910428; JP 1991-209944 19910726; JP 1991-209945 19910726; JP 1991-209946 19910726; JP 1991-209947 19910726; JP 1991-222031 19910806; JP 1991-222032 19910806; JP 1999-102878 19910726
REP No-SR.Pub; 1.Jnl.Ref; DE 3228127; EP 101185; EP 189160; GB 1158456; JP 61058560
IC ICM A61J001-00; A61J001-05; A61K009-00; A61K009-08; A61K009-107; A61K009-127; **A61K009-14**; A61K031-66; A61K037-22; A61K038-00
ICS A23D007-00; A23D007-02; A23L001-30; A61K031-00; A61K031-045; A61K031-19; A61K031-195; A61K031-23; A61K031-405; A61K031-415; A61K031-70; A61K033-00; A61K033-30; A61K035-78; A61K047-06; A61K047-12; A61K047-18; A61K047-22; B01F017-00
ICI A61K031:19, A61K031:195, A61K031:40, A61K031:405, A61K031:415, A61K031:66, A61K031:70, A61K033-30, A61K033:06, A61K033:14; A61K031:19,

A61K031:195, A61K031:40, A61K031:405, A61K031:415, A61K031:66, A61K031:70, A61K033-30, A61K033:06, A61K033:14

AB EP 510687 A UPAB: 20010421
The following are claimed (A) an infusion compsn. comprising a **sugar**, amino acids, electrolytes, a fat emulsion and a phosphate ester (I), where the compsn. is adjusted to pH 5-8 with an organic acid and where (I) is a phosphate ester of a polyhydric **alcohol** or **sugar** and is opt. in salt form, (B) a container with two separate compartments, where one compartment is filled with an infusion liq. contg. a fat emulsion and a **sugar**, and the other compartment is filled with an infusion liq. contg. amino acids and electrolytes, (C) an infusion compsn. contg. a fat emulsion and a **sugar**, where the compsn. contains 0.1-30% fat, 0.01-10% of an emulsifying agent and 5-60% of a reducing **sugar**, (D) an infusion compsn. contg. amino acids, electrolytes and (I), where the compsn. is adjusted to pH 5-8 with citric, lactic, malic, gluconic, maleic and/or malonic acid, (E) an infusion compsn. contg. a fat emulsion, a **sugar** and at least one buffer selected from L-histidine and Tris, (F) a nutrient-supplying fat emulsion obtainable by emulsifying a fat with an emulsifying agent, where the emulsion contains 0.01-5% of the emulsifying agent and has a mean droplet size of 0.17 micron or less, (G) a process for producing a nutrient-supplying fat emulsion having a mean droplet size of 0.17 micron or less, by emulsifying a fat using an emulsifying agent together with glycerol and/or **glucose**, (H) a process for stabilising a fat emulsion by mixing it with a soln. contg. divalent metal ions in the presence of citric, lactic, malic, gluconic, maleic and/or malonic acid and/or their salts.

USE - The infusion compsns. are useful for **parenteral** feedingele

Dwg.0/0

FS CPI GMPI

FA AB; DCN

ABEQ JP 05148149 A UPAB: 19931116
The transfusion comprises aminoacids of 1 to 15% (w/v), electrolytes, poly-**alcohols** or **sugar** phosphate esters as a phosphorus source, and one or more organic acids of citric acid, lactic acid, malic acid and malonic acid, with pH adjusted to 5.0 to 8.0.

Organic acid is pref. citric acid, and glycerophosphates are pref. used as phosphorus source.

USE/ADVANTAGE - Compsn. is very stable and causes no colouration or sedimentation when heated and sterilised. As the prepn. needs no mixing of aminoacids and electrolytes, it avoids bacterial contamination on mixing. The compsn. is used for nutrition supply for patients.

In an example, the transfusion comprises 1.949 g of sodium chloride, 4.302 g of potassium chloride, 2.054 g of magnesium sulphate.7H2O, 6.35 g of pottassium gluconic acid.H2O, 8.016 g of glycerophosphoric acid bipotassium (50 %), 11.340 g of sodium acetate.3H2O and 9.585 mg of zinc sulphate.7H2O (in 1 litre).

Dwg.0/0

ABEQ US 5626880 A UPAB: 19970612
A process for producing an infusion preparation comprising an infusion liquid containing a nutrient-supplying fat emulsion having a mean particle size of 0.17 mu m or less which comprises emulsifying a fat using an emulsifying agent together with one or more compounds present during the emulsification and selected from the group consisting of glycerol and **glucose**.

Dwg.0/3

ABEQ US 5674527 A UPAB: 19971119
A container with infusion liquids, which container comprises first and second compartments separated from each other by a separation means, wherein an infusion liquid containing a fat emulsion, said emulsion comprising water, a fat and an emulsifying agent, and a **sugar** is included in the first compartment and another infusion liquid containing amino acids and electrolytes is included in the second compartment.

Dwg.0/3

L102 ANSWER 50 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1992-342221 [42] WPIX
CR 1995-106650 [14]; 1995-384025 [50]; 1999-179930 [15]
DNC C1992-152111
TI New 3-step process for conditioning water-soluble substances - used for water reduction, conditioning, drying and solvent elimination.
DC B07
IN BYSTROM, K; JAKUPOVIC, E; TROFAST, E; TROFAST, J; BYSTROEM, K; TROFAST, J W; BUSTREM, K; BYSTROM, K S V K; BYSTROM, K U; TROFAST, E A
PA (ASTR) ASTRA AB; (ASTR) ASTRA PUBL AB
CYC 42
PI EP 508969 A1 19921014 (199242)* EN 14p A61K009-72
R: PT
WO 9218110 A1 19921029 (199246) EN 14p A61K009-72
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL OA SE
W: AT AU BB BG BR CA CH CS DE DK ES FI GB HU JP KP KR LK LU MG MN MW NL NO PL RO RU SD SE US
AU 9215347 A 19921117 (199310) A61K009-72
FI 9304429 A 19931008 (199351) A61K000-00
NO 9303575 A 19931006 (199403) A61K009-14 <--
EP 580648 A1 19940202 (199405) EN A61K009-72
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
HU 65095 T 19940428 (199421) A61K009-72
CZ 9302116 A3 19940413 (199422) A61K009-72
SK 9301088 A3 19940309 (199427) A61K009-72
JP 06506454 W 19940721 (199433) 5p A61K009-72
AU 662519 B 19950907 (199544) A61K009-72
EP 580648 B1 19960508 (199623) EN 7p A61K009-72
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL PT SE
DE 69210601 E 19960613 (199629) A61K009-72
ES 2086733 T3 19960701 (199633) A61K009-72
US 5562923 A 19961008 (199646) 3p A61K009-14 <--
HU 211116 B 19951030 (199732) A61K009-72
SG 43180 A1 19971017 (199801) A61K009-72
RU 2112507 C1 19980610 (199952) A61K009-14 <--
SK 280310 B6 19991108 (200003) A61K009-72
FI 105388 B1 20000815 (200047) A61K009-72
CZ 286936 B6 20000816 (200048) A61K009-72
RO 115779 B1 20000630 (200050) A61K009-72
KR 216384 B1 19990816 (200104) A61K009-72
IE 81492 B 20001227 (200110) F26B005-00
ADT EP 508969 A1 EP 1992-850062 19920324; WO 9218110 A1 WO 1992-SE186 19920324; AU 9215347 A AU 1992-15347 19920324, WO 1992-SE186 19920324; FI 9304429 A WO 1992-SE186 19920324, FI 1993-4429 19931008; NO 9303575 A WO 1992-SE186 19920324, NO 1993-3575 19931006; EP 580648 A1 EP 1992-907877 19920324, WO 1992-SE186 19920324; HU 65095 T WO 1992-SE186 19920324, HU 1993-2870 19920324; CZ 9302116 A3 CZ 1993-2116 19920324; SK 9301088 A3 WO 1992-SE186 19920324, SK 1993-1088 19931008; JP 06506454 W JP 1992-507195 19920324, WO 1992-SE186 19920324; AU 662519 B AU 1992-15347 19920324; EP 580648 B1 EP 1992-907877 19920324, WO 1992-SE186 19920324; DE 69210601 E DE 1992-610601 19920324, EP 1992-907877 19920324, WO 1992-SE186 19920324; ES 2086733 T3 EP 1992-907877 19920324; US 5562923 A Cont of US 1993-129204 19931025, US 1995-479494 19950607; HU 211116 B WO 1992-SE186 19920324, HU 1993-2870 19920324; SG 43180 A1 SG 1996-4975 19920324; RU 2112507 C1 WO 1992-SE186 19920324, RU 1993-58260 19920324; SK 280310 B6 WO 1992-SE186 19920324, SK 1993-1088 19920324; FI 105388 B1 WO 1992-SE186 19920324, FI 1993-4429 19931008; CZ 286936 B6 WO 1992-SE186 19920324, CZ 1993-2116 19920324; RO 115779 B1 WO 1992-SE186 19920324, RO 1993-1336 19920324; KR 216384 B1 WO 1992-SE186 19920324, KR 1993-703065 19931009; IE 81492 B IE 1992-1144 19920410
FDT AU 9215347 A Based on WO 9218110; EP 580648 A1 Based on WO 9218110; HU 65095 T Based on WO 9218110; JP 06506454 W Based on WO 9218110; AU 662519 B Previous Publ. AU 9215347, Based on WO 9218110; EP 580648 B1 Based on WO 9218110; DE 69210601 E Based on EP 580648, Based on WO 9218110; ES 2086733 T3 Based on EP 580648; HU 211116 B Previous Publ. HU 65095, Based on WO 9218110; SK 280310 B6 Previous Publ. SK 9301088; FI 105388 B1 Previous

Publ. FI 9304429; CZ 286936 B6 Previous Publ. CZ 9302116, Based on WO 9218110; RO 115779 B1 Based on WO 9218110
PRAI SE 1991-1090 19910411
REP EP 436110; US 4405598; WO 8607547
IC ICM A61K000-00; **A61K009-14**; A61K009-72; F26B005-00
ICS A61K031-135; A61K031-70; F26B003-00
AB EP 508969 A UPAB: 20010220
Prepn. of water-soluble micronised substances, which can be produced, stored and used while maintaining the aerodynamic properties required for inhalation, comprises: (a) reducing, if necessary, the residual water from the micronised substance (MS) by drying opt. at an elevated temp. and/or vacuum; (b) conditioning with a solvent; and (c) eliminating residual solvent by storing in a dry place like vacuum or by purging with an inert gas.
USE/ADVANTAGE - Used for substances such as additives e.g. **carbohydrates** and aminoacids or drugs pref. antiasthmatic or antiallergic substances. The process is reliable and the desired polymorphic form e.g. crystalline form, can be conveniently and reproducibly prepd. The particle size of the MS is identical before and after conditioning which rearranges the outer layer of the crystals or the **amorphous** substances giving a more stable and less hygroscopic prod. The prods. have improved physicochemical properties in the dry state, facilitating the technical handling and increasing the medical value of the substances. Unconditioned spray-dried **lactose** gave off 40-44 J/g energy compared with less than 0.1 J/g for spray dried **lactose** conditioned in EtOH vapour for 100 h
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B07-A02; B10-A07; B12-D02; B12-K02
ABEQ EP 580648 B UPAB: 19960610
A process for providing water-soluble micronised substances having a particle size of less than 10 micrometers, which can be produced, stored and used while maintaining the aerodynamic properties for inhalation of such substances, characterised in (a) reducing, if necessary, the residual water from the micronised substance by drying optionally at an elevated temperature and/or vacuum, (b) conditioning said dried, micronised substances with a solvent, and (c) eliminating residual solvent by storing in a dry place like vacuum or by purging with an inert gas.
Dwg.0/0
ABEQ US 5562923 A UPAB: 19961115
A process for preparing a water-soluble micronised active agent or pharmaceutical additive of improved stability, said process comprising:a) reducing if necessary the residual water content of the micronised active agent or pharmaceutical additive; b) conditioning the dry micronised active agent or pharmaceutical composition with a solvent, and c) eliminating residual solvent.
Dwg.0/0

L102 ANSWER 51 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1992-234345 [28] WPIX
DNC C1992-105656
TI Lyophilised aminoacid compsns. with high glutamine content - have high stability, density and flowability, rapidly rehydrated for **injection** with water or **glucose** soln..
DC B05
IN TORRE, A
PA (TORR-N) TORRE FARM SRL A
CYC 49
PI WO 9210175 A1 19920625 (199228)* EN 10p A61K031-195
RW: AT BE BF BJ CF CG CH CI CM DE DK ES FR GA GB GN GR IT LU MC ML MR NL SE SN TD TG
W: AU BB BG BR CA CS FI HU JP KP KR LK MG MN MW NO PL RO SD SU US
AU 9190384 A 19920708 (199241) A61K031-195
EP 561866 A1 19930929 (199339) EN A61K031-195
R: BE CH DE FR GB IT LI NL SE

IT 1244880 B 19940912 (199508) A61K000-00
EP 561866 B1 19950830 (199539) EN 5p A61K031-195
R: BE CH DE FR GB IT LI NL SE
DE 69112642 E 19951005 (199545) A61K031-195
ADT WO 9210175 A1 WO 1991-EP2352 19911209; AU 9190384 A AU 1991-90384 19911209, WO 1991-EP2352 19911209; EP 561866 A1 WO 1991-EP2352 19911209, EP 1992-900368 19911209; IT 1244880 B IT 1990-22342 19901211; EP 561866 B1 WO 1991-EP2352 19911209, EP 1992-900368 19911209; DE 69112642 E DE 1991-612642 19911209, WO 1991-EP2352 19911209, EP 1992-900368 19911209
FDT AU 9190384 A Based on WO 9210175; EP 561866 A1 Based on WO 9210175; EP 561866 B1 Based on WO 9210175; DE 69112642 E Based on EP 561866, Based on WO 9210175
PRAI IT 1990-22342 19901211
REP WO 8701589; 03Jnl.Ref
IC ICM A61K031-195
ICS **A61K009-14**
AB WO 9210175 A UPAB: 19931006
Compsns. are in the form of sterile powder to be dissolved in sterile **injectable** solns. before use. Pref. amt. of glutamine is up to 70% (20-50%). The compsns. have a density of at least 0.3 g/ml, a solubility of 10% in water and at least 5% in 5-50% **glucose** soln., a stability of more than 12 months at room temp. when dry and more than 15 hrs. at room temp. or more than 48 hrs. at 4 deg.C in reconstituted soln. The soln. has a microparticle count below these limits: 1000 particles of at least 2 micron; 100 particles of at least 5 micron; 50 particles of at least 10 micron; and 4 particles of at least 20 micron. Prepn. comprises (a) solubilisation of the amino acids and glutamine in water for **injection**; (b) filtration of the soln. through a sterile membrane at room temp.; (c) freeze drying the filtrate; and (d) distributing the solid into sterile containers under N2.
ADVANTAGE - Used with glucides, lipids, vitamins and mineral salts w.r.t. nutritional needs.
FS CPI
FA AB; DCN
MC CPI: B10-B02J; B12-J01
ABEQ EP 561866 A UPAB: 19931123
Compsns. are in the form of sterile powder to be dissolved in sterile **injectable** solns. before use. Pref. amt. of glutamine is up to 70% (20-50%). The compsns. have a density of at least 0.3 g/ml, a solubility of 10% in water and at least 5% in 5-50% **glucose** soln., a stability of more than 12 months at room temp. when dry and more than 15 hrs. at room temp. or more than 48 hrs. at 4 deg.C in reconstituted soln. The soln. has a microparticle count below these limits: 1000 particles of at least 2 micron; 100 particles of at least 5 micron; 50 particles of at least 10 micron; and 4 particles of at least 20 micron. Prepn. comprises (a) solubilisation of the aminoacids and glutamine in water for **injection**; (b) filtration of the soln. through a sterile membrane at room temp.; (c) freeze drying the filtrate; and (d) distributing the solid into sterile containers under N2.
ADVANTAGE - Used with glucide, lipids, vitamins and mineral salts w.r.t. nutritional need.
ABEQ EP 561866 B UPAB: 19951004
Amino acids compositions by **parenteral** administration, containing glutamine in amounts from 20 to 50% by weight in form of sterile lyophilized powder, to be dissolved in sterile **injectable** solutions before use, said powder having a density at least 0.3 g/ml, a solubility of 10% in water and at least of 5% in **glucose** solutions with **glucose** concentrations ranging from 5 to 50%, stability longer than 12 months at room temperature in the dry state and longer than 15 hours at room temperature or longer than 48 hours at 4deg.C, in reconstituted solution, said solution having a microparticle count lower than these limits: 1,000 particles at least 2 microm 100 particles at least 5 microm 50 particles at least 10 microm 4 particles at least 20 microm.
Dwg.0/0

L102 ANSWER 52 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1992-183387 [22] WPIX
CR 1992-183386 [22]; 1992-183403 [22]
DNC C1992-083975
TI Lyophilised prepn. for antiinflammatory - contg. **maltose** drying aid for prodn. of emulsions of lipophilic antiallergic drugs for **parenteral** admin..
DC B02 B07
IN SEKI, J; TAKAHASHI, Y; USHIMARU, K; YAMAMOTO, H; YAMANE, S
PA (NNSH) NIPPON SHINYAKU CO LTD
CYC 25
PI WO 9207552 A1 19920514 (199222)* JA 27p A61K009-14 <--
RW: AT BE CH DE DK ES FR GB GR IT LU NL SE
W: AU BR CA FI HU JP KR NO SU US
AU 9187667 A 19920526 (199235) A61K009-14 <--
JP 03517232 X 19921105 (199251) 19p A61K009-14 <--
EP 556394 A1 19930825 (199334) EN 11p A61K009-14 <--
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
HU 64864 T 19940328 (199417) A61K047-26
AU 665931 B 19960125 (199611) A61K009-107
US 5635491 A 19970603 (199728) 8p A61K031-70
JP 2626247 B2 19970702 (199731) 7p A61K009-14 <--
RU 2097025 C1 19971127 (199831) 10p A61K009-14 <--
CA 2095627 C 19990105 (199912) A61K009-14 <--
KR 154343 B1 19981116 (200029) A61K009-14 <--
HU 217808 B 20000428 (200030) A61K047-26
ADT WO 9207552 A1 WO 1991-JP1509 19911105; AU 9187667 A AU 1991-87667 19911105, WO 1991-JP1509 19911105; JP 03517232 X JP 1991-517232 19911105, WO 1991-JP1509 19911105; EP 556394 A1 EP 1991-918946 19911105, WO 1991-JP1509 19911105; HU 64864 T WO 1991-JP1509 19911105, HU 1993-1323 19911105; AU 665931 B AU 1991-87667 19911105; US 5635491 A WO 1991-JP1509 19911105, US 1993-50216 19930621; JP 2626247 B2 JP 1991-517232 19911105, WO 1991-JP1509 19911105; RU 2097025 C1 WO 1991-JP1509 19911105, RU 1993-32313 19930505; CA 2095627 C CA 1991-2095627 19911105; KR 154343 B1 KR 1993-701344 19930504; HU 217808 B WO 1991-JP1509 19911105, HU 1993-1323 19911105
FDT AU 9187667 A Based on WO 9207552; JP 03517232 X Based on WO 9207552; EP 556394 A1 Based on WO 9207552; HU 64864 T Based on WO 9207552; AU 665931 B Previous Publ. AU 9187667, Based on WO 9207552; US 5635491 A Based on WO 9207552; JP 2626247 B2 Based on WO 9207552; HU 217808 B Previous Publ. HU 64864, Based on WO 9207552
PRAI JP 1990-301639 19901106; JP 1990-301640 19901106; JP 1990-312056 19901116
REP EP 315079; JP 01249716; JP 02000203; JP 62029513
IC ICM A61K009-107; **A61K009-14**; A61K031-70; A61K047-26
ICS A61K009-10; A61K009-19; A61K031-40; A61K031-415; A61K031-44; A61K031-57; A61K031-71; A61K037-02; C07H001-00
AB WO 9207552 A UPAB: 20000624
Prepn. is produced by including **maltose** in a fat emulsion prior to lyophilisation. Reconstitution of the emulsion from the lyophilised prepn. gives a fat emulsion having emulsion particles of mean dia. 10-100 nm.

USE/ADVANTAGE - Used for antiallergics, vitamins, antibiotics, anticancers, antivirals, antihypertensives, radical inhibitors, **vaccines** and tranquillisers. The prepn. has high temp. stability and the redissolution of the lyophilised material is complete and rapid, c.f. use of other sugars as drying aids.

In an example, dexamethasone palmitate (3g), purified soya oil (50g) and egg yolk lecithin (20g) are mixed at 60 deg.C. 10% aq. soln. of **maltose** (500ml) is added and the mixt. emulsified in a homomixer, then further emulsified at high pressure in a homogeniser to give an emulsion with mean particle dia. of 10-100 nm. This emulsion is conventionally lyophilised. Redissolution of the dried lyophilisate by addn. of water is rapid and complete and after soln. the emulsion particle dia. range is similar to that prior to lyophilisation.
0/0

FS CPI
FA AB; DCN
MC CPI: B02-V02; B02-Z; B03-L; B07-A02; B12-C10; B12-D02; B12-D07; B12-F05; B12-G07; B12-M03
ABEQ EP 556394 A UPAB: 19931119
Prepn. is produced by including **maltose** in a fat emulsion prior to lyophilisation. Reconstitution of the emulsion from the lyophilised prepn. gives a fat emulsion having emulsion particles of mean dia. 10-100 nm.

USE/ADVANTAGE - Used for antiallergics, vitamins, antibiotics, antitumour agents, antivirals, antihypertensives, radical inhibitors, **vaccines** and tranquillisers. The prepn. has high temp. stability and the redissolution of the lyophilised material is complete and rapid, c.f. use of other sugars as drying aids.

In an example, dexamethasone palmitate (3g), purified soya oil (50g) and egg yolk lecithin (20g) are mixed at 60 deg.C. 10% aq. soln. of **maltose** (500ml) is added and the mixt. emulsified in a homomixer, then further emulsified at high pressure in a homogeniser to give an emulsion with mean particle dia. of 10-100 nm. This emulsion is conventionally lyophilised. Redissolution of the dried lyophilisate by addn. of water is rapid and complete and after soln. the emulsion particle dia. range is similar to that prior to lyophilisation.
Dwg.0/0
ABEQ US 5635491 A UPAB: 19970709
A stable lyophilised composition, capable of reconstituting a fatty emulsion in which the mean particle size is 10-100 nm without substantial enlargement of the particle size between prior to lyophilisation and after reconstitution with water, which comprises lyophilised lipid emulsion particles for a fatty emulsion wherein said particles comprise a therapeutically effective amount of a therapeutic active substance or a diagnostically effective amount of a diagnostic agent and an amount of **maltose** effective, upon dispersion of said lyophilised composition in water, to produce a fatty emulsion in which the mean emulsion particle size is 10-100 nm, without substantial enlargement of the particle size between prior to lyophilisation add after reconstitution with water, under conditions of storage at elevated temperatures up to 40 deg. C. or the accelerated heating equivalent thereof.
Dwg.0/0

L102 ANSWER 53 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1991-353179 [48] WPIX
CR 1990-297515 [39]
DNC C1991-152308
TI Compsn. of procaine and complexing agent, e.g. ascorbic acid - for treating Alzheimer's disease, age-related conditions, e.g. tinnitus, and withdrawal symptoms of narcotic addiction.
DC B02 B07
IN SAPSE, A T
PA (SPEC-N) SPECTRUM PHARM CORP
CYC 1
PI US 5064858 A 19911112 (199148)*
ADT US 5064858 A US 1990-578030 19900905
PRAI US 1988-233247 19880817; US 1990-578030 19900905
IC **A61K009-14**; A61K031-21
AB US 5064858 A UPAB: 19930928
The compsn. comprises procaine (1-10%), a complexing agent (e.g. 0.25-10% ascorbic acid) and opt. lidocaine, zinc citrate, an anticholinesterase, or an anticortisol agent (e.g. dilantin or clonidine), etc.. Other possible complexing agents are acetylsalicylic acid (for treating Alzheimer's disease), **polysaccharides**, glycols, pantothenic acid, amino acids and caffeine.

USE/ADVANTAGE - The compsn. is used to reduce the withdrawal symptoms of individuals addicted to narcotics or to treat the symptoms of age-related conditions such as tinnitus and Alzheimer's disease. It may be administered orally, **parenterally** or intravenously. An oral dosage unit contains 25-300 mg of procaine, and a **parenteral**

dosage unit contains 25-100 mg of procaine.

In an example, 11 individuals having chronic and recurring addiction to cocaine are treated with a formulation comprising a protected complex of 4% procaine complexed with ascorbic acid. Dosage is 200-300 mg/day. After 3 weeks, 9 of the addicts avoid the use of cocaine or other narcotics for 3-7 months. Furthermore, attempts to use cocaine during the three-week period lead to aversion symptoms including vomiting, abdominal pain and muscle cramps. @(5pp Dwg.No.0/0)

FS CPI
FA AB; DCN
MC CPI: B03-F; B04-A06; B04-C02; B05-A03A; B07-D04A; B07-D09; B10-B01A; B10-B02; B10-C02; B10-C03; B10-C04D; B10-E04C; B12-C09; B12-G01B1; B12-G01B3; B12-G04; B12-J05; B12-L04

L102 ANSWER 54 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1991-319156 [44] WPIX
DNC C1991-137902
TI Ultrasound contrast agent, **vaccine**, diagnostic or therapeutic agent - comprising micro-particulate polyelectrolyte complex and at least one active agent.
DC A96 B04 B07 D16
IN GRONER, A; HOFFMANN, D; KRONE, V; MAGERSTADT, M; WALCH, A; GROENER, A; MAGERSTAEDT, M
PA (FARH) HOECHST AG
CYC 16
PI

EP 454044	A	19911030 (199144)*				
R: AT BE CH DE ES FR GB IT LI NL SE						
DE 4013110	A	19911031 (199145)				
CA 2041093	A	19911026 (199203)				
DE 4035187	A	19920507 (199220)		7p		
JP 04225915	A	19920814 (199239)		7p	A61K009-14	<--
EP 454044	A3	19930113 (199346)				
EP 454044	B1	19951206 (199602)	DE	11p	A61K009-14	<--
R: AT BE CH DE DK ES FR GB IT LI NL SE						
DE 59107006	G	19960118 (199608)			A61K009-14	<--
ES 2081384	T3	19960301 (199616)			A61K009-14	<--
IE 70747	B	19961230 (199707)			A61K009-50	
US 5700459	A	19971223 (199806)		6p	A61K009-14	<--
JP 3168215	B2	20010521 (200130)		6p	A61K009-14	<--

ADT EP 454044 A EP 1991-106495 19910423; DE 4013110 A DE 1990-4013110 19900425; DE 4035187 A DE 1990-4035187 19901106; JP 04225915 A JP 1991-119126 19910424; EP 454044 A3 EP 1991-106495 19910423; EP 454044 B1 EP 1991-106495 19910423; DE 59107006 G DE 1991-507006 19910423, EP 1991-106495 19910423; ES 2081384 T3 EP 1991-106495 19910423; IE 70747 B IE 1991-1369 19910424; US 5700459 A Cont of US 1991-689643 19910423, Cont of US 1993-88581 19930709, US 1994-341164 19941116; JP 3168215 B2 JP 1991-119126 19910424
FDT DE 59107006 G Based on EP 454044; ES 2081384 T3 Based on EP 454044; JP 3168215 B2 Previous Publ. JP 04225915
PRAI DE 1990-4013110 19900425; DE 1990-4035187 19901106
REP NoSR.Pub; BE 901704; EP 152898; EP 388758; EP 392487; GB 1183403; GB 2153780
IC ICM **A61K009-14**; A61K009-50
ICS A61K009-107; A61K009-16; A61K031-71; A61K031-72; A61K037-02; A61K038-00; A61K039-00; A61K039-205; A61K045-00; A61K047-36; A61K047-42; A61K049-00
AB EP 454044 A UPAB: 19940103
A pharmaceutical compsn. contains a polyelectrolyte complex in microparticular form and at least one active agent. The active agent is pref. active peptide, protein, enzyme, enzyme inhibitor, antigen, cytostatic, antiinflammatory, antibiotic, **vaccine**, and optional additives such as adjuvants, amphiphilic molecules etc. The polyelectrolyte pref. contains at least two components including a polymer, e.g. xylan polysulphate, **dextran** sulphate, polyaminoacd, **polysaccharide** polysulphate, insulin, hydroxyethyl starch, **polysaccharide** polysulphonate, polyphosphate,

polysaccharide polyphosphate, poly-L-lysine, poly alpha, beta-(2-dimethylamino ethyl)-D,L-aspartamide, chitosan, lysine octadecyl ester, or aminated **dextran**, cyclodextrin, cellulose ether or pectin and derivs., especially hydrophobised polybase derivs. The polyelectrolyte particles have an average size of up to 5 microns or less than 15 microns or less than 100 microns and are formed by mixing aq. sols. of acidic and basic components.

USE/ADVANTAGE - The compsn. is used as an ultrasound contrast agent, **vaccines**, or diagnostic or therapeutic agents. They can be administered orally or **parenterally**. The active agent is either one of the polyelectrolyte components or a cpd. which is chemically bound to or adsorbed on the microparticles. The polyelectrolyte releases the active ingredient slowly over time. The microparticles are easily produced. @(9pp Dwg.No.0/0)

0/0

FS CPI

FA AB; DCN

MC CPI: A12-M01; A12-M02; A12-V01; B02-V02; B02-Z; B04-B02C; B11-C08; B12-K04C; D05-H07; D05-H09

ABEQ EP 454044 A UPAB: 19940103

A pharmaceutical compsn. contains a polyelectrolyte complex in microparticular form and at least one active agent. The active agent is pref. active peptide, protein, enzyme, enzyme inhibitor, antigen, cytostatic, antiinflammatory, antibiotic, **vaccine**, and optional additives such as adjuvants, amphiphilic molecules etc. The polyelectrolyte pref. contains at least two components including a polymer, e.g. xylan polysulphate, **dextran** sulphate, polyaminoacd, **polysaccharide** polysulphate, insulin, hydroxyethyl starch, **polysaccharide** polysulphonate, polyphosphate, **polysaccharide** polyphosphate, poly-L-lysine, poly alpha, beta-(2-dimethylamino ethyl)-D,L-aspartamide, chitosan, lysine octadecyl ester, or aminated **dextran**, cyclodextrin, cellulose ether or pectin and derivs., especially hydrophobised polybase derivs. The polyelectrolyte particles have an average size of up to 5 microns or less than 15 microns or less than 100 microns and are formed by mixing aq. sols. of acidic and basic components.

USE/ADVANTAGE - The compsn. is used as an ultrasound contrast agent, **vaccines**, or diagnostic or therapeutic agents. They can be administered orally or **parenterally**. The active agent is either one of the polyelectrolyte components or a cpd. which is chemically bound to or adsorbed on the microparticles. The polyelectrolyte releases the active ingredient slowly over time. The microparticles are easily produced. @(9pp Dwg.No.0/0)

ABEQ EP 454044 B UPAB: 19960115

A pharmaceutical composition in microparticulate form containing a polyelectrolyte complex of polycations with polyanions and at least one additional active substance.

Dwg.0/0

ABEQ US 5700459 A UPAB: 19980209

A pharmaceutical compsn. contains a polyelectrolyte complex in microparticular form and at least one active agent. The active agent is pref. active peptide, protein, enzyme, enzyme inhibitor, antigen, cytostatic, antiinflammatory, antibiotic, **vaccine**, and optional additives such as adjuvants, amphiphilic molecules etc. The polyelectrolyte pref. contains at least two components including a polymer, e.g. xylan polysulphate, **dextran** sulphate, polyaminoacd, **polysaccharide** polysulphate, insulin, hydroxyethyl starch, **polysaccharide** polysulphonate, polyphosphate, **polysaccharide** polyphosphate, poly-L-lysine, poly alpha, beta-(2-dimethylamino ethyl)-D,L-aspartamide, chitosan, lysine octadecyl ester, or aminated **dextran**, cyclodextrin, cellulose ether or pectin and derivs., especially hydrophobised polybase derivs. The polyelectrolyte particles have an average size of up to 5 microns or less than 15 microns or less than 100 microns and are formed by mixing aq. sols. of acidic and basic components.

USE/ADVANTAGE - The compsn. is used as an ultrasound contrast agent,

vaccines, or diagnostic or therapeutic agents. They can be administered orally or **parenterally**. The active agent is either one of the polyelectrolyte components or a cpd. which is chemically bound to or adsorbed on the microparticles. The polyelectrolyte releases the active ingredient slowly over time. The microparticles are easily produced.
Dwg.0/0

L102 ANSWER 55 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1991-222636 [30] WPIX
CR 1993-386168 [48]; 1996-442370 [44]
DNC C1991-096659
TI Prepn. of delivery **matrix** or unit dosage form - comprises solidifying **matrix** compsn. dissolved or dispersed in first solvent then contacting with second solvent.
DC B07 P33
IN CARBONE, J; DAVIES, J D; GOLE, D J; LEVINSON, R S; CARBONNE, J
PA (JANC) JANSSEN PHARM INC; (MEDI-N) MEDIVENTURES INC; (GOLE-I) GOLE D J
CYC 20
PI

WO 9109591	A	19910711 (199130)*				
RW: AT BE CH DE DK ES FR GB GR IT LI LU NL SE						
W: AU CA JP KR						
AU 9171711	A	19910724 (199143)				
EP 460185	A	19911211 (199150)				
R: AT BE CH DE ES FR GB GR IT LI LU NL SE						
US 5120549	A	19920609 (199226)	13p	A61K009-14	<--	
JP 04503959	W	19920716 (199235)	16p	A61K009-14	<--	
DK 9100703	A	19921019 (199306)#		A61K009-20		
US 5215756	A	19930601 (199323)	12p	A61K009-14	<--	
AU 646428	B	19940224 (199413)		A61K009-14	<--	
US 5330763	A	19940719 (199428)	12p	A61K009-14	<--	
US 5330764	A	19940719 (199428)	13p	A61K009-14	<--	
SG 49249	A1	19980518 (199835)		A61K009-14	<--	
EP 460185	B1	19990303 (199913) EN		A61K009-14	<--	
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE						
DE 69032976	E	19990408 (199920)		A61K009-14	<--	
ES 2131049	T3	19990716 (199935)		A61K009-14	<--	
KR 173989	B1	19990201 (200039)		A61K009-14	<--	
JP 3107566	B2	20001113 (200060)	14p	A61K009-14	<--	

ADT EP 460185 A EP 1991-902009 19901211; US 5120549 A CIP of US 1989-454938 19891222, Cont of US 1990-613087 19901106, US 1991-734635 19910723; JP 04503959 W WO 1990-US7319 19901211, JP 1991-502774 19901211; DK 9100703 A DK 1991-703 19910418; US 5215756 A CIP of US 1989-454938 19891222, US 1990-613087 19901106; AU 646428 B AU 1991-71711 19901211; US 5330763 A CIP of US 1989-454938 19891222, Cont of US 1990-613087 19901106, US 1991-734505 19910723; US 5330764 A CIP of US 1989-454938 19891222, Cont of US 1990-613087 19901106, US 1991-734635 19910723; SG 49249 A1 SG 1996-8328 19901211; EP 460185 B1 WO 1990-US7319 19901211, EP 1991-902009 19901211; DE 69032976 E DE 1990-632976 19901211, WO 1990-US7319 19901211, EP 1991-902009 19901211; ES 2131049 T3 EP 1991-902009 19901211; KR 173989 B1 WO 1990-US7319 19901211, KR 1991-700954 19910821; JP 3107566 B2 WO 1990-US7319 19901211, JP 1991-502774 19901211
FDT JP 04503959 W Based on WO 9109591; AU 646428 B Previous Publ. AU 9171711, Based on WO 9109591; US 5330763 A Cont of US 5215756; US 5330764 A Cont of US 5215756; EP 460185 B1 Based on WO 9109591; DE 69032976 E Based on EP 460185, Based on WO 9109591; ES 2131049 T3 Based on EP 460185; JP 3107566 B2 Previous Publ. JP 04503959, Based on WO 9109591
PRAI US 1990-613087 19901106; US 1989-454938 19891222; US 1991-734635 19910723; DK 1991-703 19910418; US 1991-734505 19910723
REP DE 2822882; EP 394050; GB 1310824; GB 2114440; US 4305502; US 4818542; WO 8804551
IC ICM **A61K009-14**; A61K009-20
ICS A01N025-10; A23G003-00; A23L001-22; A61J003-06; A61K007-16; A61K047-36; A61K047-38; A61K047-42; C05G005-00
AB WO 9109591 A UPAB: 20001123
Prepn. of a delivery matrix or a unit dosage form comprises: (a)

solidifying a dispersion or soln. (or a unit vol. of the dispersion or soln.) of a matrix forming agent in a first solvent, and (b) contacting the solidified dispersion or soln. (or unit vol.) with a second solvent. The first solvent is miscible with the second solvent. The second solvent is at a temp. at or higher than the solidification point of the second solvent and a temp. at or lower than the solidification point of the first solvent.

The matrix forming agent is insoluble in the second solvent. The contacting is sufficient to remove the first solvent from the solidified dispersion or soln. (or unit vol.) thereby yielding a delivery matrix that is free of the first solvent.

USE/ADVANTAGE - The dosage forms have potential applications in pharmaceuticals, food, veterinary fields, cosmetics, diagnostics, sanitary fields, in reconstitutable carrier units for pigmented applcn. for paint and other artistic uses and in agricultural and horticultural prods. requiring release of active ingredients in the presence of water or rain. The dosage form have quick dissolution and disintegration, pleasant taste and mouthfeel, nutritional value, low calorie content and noncariogenicity. @(61pp Dwg.No.0/0)

FS CPI GMPI

FA AB; DCN

MC CPI: B04-B02C2; B04-B02C3; B04-B04A4; B04-B04A6; B04-C02; B04-C03A; B05-A01B; B05-C07; B06-D18; B06-F01; B07-A02; B07-D04C; B10-A07; B10-B02; B10-B03B; B10-E04A; B11-C04; B12-J01; B12-K04; B12-L02; B12-L09; B12-L10

ABEQ US 5120549 A UPAB: 19930928

A new method for prepn. of a porous delivery matrix comprises (a) solidifying a dispersion or soln. of matrix-forming agent in a 1st solvent, (b) contacting this with a 2nd solvent, the 1st solvent being miscible with the 2nd, but of higher solidifying pt. than the 2nd and the 2nd solvent being at a temp. at or above its solidification pt., but below the solidification pt. of the 1st, and with the matrix forming agent insol. in the 2nd solvent. The 1st solvent is removed from the solidified dispersion or soln., giving matrix free of solvent, which is recovered. The 2nd solvent may then be evapd. from the matrix or removed by contacting with more volatile addn. solvents.

Matrix forming agents include gelatin, pectin, **mannitol** and glycine and comprise 0.1-15% wt. of dispersion or soln. The dispersion or soln. may contain an active agent insol. the 2nd solvent. A porous foam dosage form may be obtd. by forming and maintaining a gas dispersed in the matrix.

ADVANTAGE - Avoids cracking and melting in lyophilisation and gives durable form of adequate strength and porosity.

0/0

ABEQ US 5215756 A UPAB: 19931115

A porous unit dosage form is prepd. by (a) dispersing or dissolving a matrix forming agent in a first solvent; (b) solidifying a unit volume of the dispersion or soln., (c) contacting the mixt. volume with a second solvent which is miscible with the first solvent and with a lower solidification pt. The temp. of the second solvent lies between the solidification pts. of the two solvents. The matrix forming agent is insol. in the second solvent. The contacting removes the first solvent from the unit volume; and (d) recovering the unit dosage form, the matrix forming agent being present in the soln. or dispersion in a sufficient amt. to form a matrix when the first solvent is removed.

Pref. the 1st solvent is water and the 2nd is a water miscible alcohol. The matrix forming agent is e.g. gelatin, dextrin, soy protein, wheat protein, psyllium seed protein, gum, alginates etc.. Pref. the method comprises an additional step of evaporating the residual 2nd from the unit dosage form.

USE/ADVANTAGE - Solid solvent from a solidified mixt. is removed with reduced cracking of the final prepn.. The prepn. may be used in pharmaceutical, food, veterinary, cosmetic, diagnostic and sanitary applications.

Dwg.0/0

ABEQ US 5330763 A UPAB: 19940831

Porous unit dosage form is prepd. by (a) dispersing or dissolving a matrix forming agent(MFA) in a solvent; (b) solidifying a unit vol. of the mixt., (c) contacting with a second solvent (which is miscible with and which has a lower solidification point than the first) at least at the solidification point(SP) of the second solvent but below the SP of the first solvent, to remove the first solvent, yielding a unit dosage form; and (d) recovering the dosage form.

The MFA is insol. in the second solvent, and is pref. e.g. a gelatin, dextrin or carrageenan, cellulose, wheat gluten and/or papain etc..

USE/ADVANTAGE - The method is inexpensive and reduces the incident of cracking of the final prod. and of meltback during the process. As a dosage form for pharmaceuticals, nutrients, diagnostics, confectionaries, fertilisers or insecticides.

Dwg.0/0

ABEQ US 5330764 A UPAB: 19940831

Prepn of a porous delivery matrix comprises solidifying a dispersion of a soln of a matrix former from a 1st solvent, contacting with a 2nd solvent miscible with the 1st, the solidification pt being higher in the 1st, the 2nd solvent being at temp above the solidification pt of the 2nd but below that of the 1st and the matrix former being insol in the 2nd.

The 1st solvent is removed to give a delivery matrix free of solvent on recovery, eg by evapn the 2nd solvent or by contacting with a more volatile 3rd solvent.

Matrix formers at concn of 0.1-15% wt include gelatins, dextrins, soy, wheat and psyllium proteins, gums, alginates, **polysaccharides**, COOMe- and OHEt-celluloses, 2-12C aminoacid, etc. The dispersion soln may contain active agents recovered as foam dosage form to which further active agents may be added.

ADVANTAGE - Uses simpler equipment than conventional freeze drying or lyophilisation. More easily taken and rapidly dissolved in stomach than hard ampoules.

Dwg.0/0

L102 ANSWER 56 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1991-038546 [06] WPIX
DNC C1991-016488
TI **Micronising** slightly-soluble drug - by mixing with **sugar** or **sugar alcohol** and subjecting to high-speed stirring or impact comminution.
DC B07 P33
IN KOBAYASHI, M; NODA, K; OSAWA, T; SAMEJIMA, M
PA (TANA) TANABE SEIYAKU KK; (TANA) TANABE SEIYAKU CO
CYC 18
PI EP 411629 A 19910206 (199106)* 7p
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
JP 03066613 A 19910322 (199118)
CA 2022465 A 19910205 (199128)
US 5202129 A 19930413 (199317) 5p A61K009-14 <--
EP 411629 B1 19931103 (199344) EN 7p A61K009-14 <--
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
DE 69004372 E 19931209 (199350) A61K009-14 <--
ES 2062221 T3 19941216 (199505) A61K009-14 <--
JP 2642486 B2 19970820 (199738) 5p A61K009-14 <--
CA 2022465 C 19980421 (199827) A61K009-14 <--
KR 126465 B1 19971224 (199952) A61K009-14 <--
ADT EP 411629 A EP 1990-114858 19900802; JP 03066613 A JP 1989-204132 19890804; US 5202129 A US 1990-563091 19900803; EP 411629 B1 EP 1990-114858 19900802; DE 69004372 E DE 1990-604372 19900802, EP 1990-114858 19900802; ES 2062221 T3 EP 1990-114858 19900802; JP 2642486 B2 JP 1989-204132 19890804; CA 2022465 C CA 1990-2022465 19900801; KR 126465 B1 KR 1990-11858 19900802
FDT DE 69004372 E Based on EP 411629; ES 2062221 T3 Based on EP 411629; JP 2642486 B2 Previous Publ. JP 03066613
PRAI JP 1989-204132 19890804
REP 2.Jnl.Ref; A3...9119; FR 2108032; FR 2162245; FR 2257266; GB 2159407; GB 2224207; NoSR.Pub

IC A61J003-02; **A61K009-14**; A61K047-26
ICM **A61K009-14**
ICS A61J003-02; A61K009-16; A61K047-26
AB EP 411629 A UPAB: 19930928
Micronising a slightly-soluble drug comprises subjecting a mixt. of the drug and a **sugar** or **sugar alcohol** to high-speed stirring comminution or impact comminution. Pharmaceutical formulation comprises the obtd. micronised drug as active ingredient together with suitable excipients or diluents.
ADVANTAGE - Micronisation improves the solubility and bioavailability of the drug in the gastrointestinal tract, without the need for chemical modification or potentially toxic organic solvents. The alteration of the crystalline structure of the drug is slight or moderate, and the process is simple and inexpensive.
0/0
FS CPI GMPI
FA AB; DCN
MC CPI: B07-A02; B10-A07; B10-C03; B12-C10; B12-D04; B12-D06; B12-D07; B12-E02; B12-F01; B12-F05; B12-F07; B12-G03
ABEQ US 5202129 A UPAB: 19931025
Micronising a slightly soluble drug (D), comprises high-speed stirring comminution or impact comminution (to give micronised drug of ave dia less than 1 micron) of a mixt of (D) and a **sugar** or **sugar alcohol**. The **sugar** cpd. pref has a mol. wt. of less than 500 and is esp. xylitol, **mannitol**, **sorbitol**, arabinose, rebose, xylose, **glucose**, **mannose**, galactose, **sucrose** and **lactose**. The ratio **sugar** cpd. is 2.5-50 pts.wt. per pt.wt. (D).
USE/ADVANTAGE - Micronisation barely alters crystal form of the drug. The operation is safe since no organic solvent is used, the prodn. cost is low and the operation is easy.
Dwg.0/0
ABEQ EP 411629 B UPAB: 19931213
A process for micronising a slightly-soluble drug characterised by subjecting a mixture of said drug in a **sugar** or **sugar alcohol** to high-speed stirring comminution or impact comminution, wherein the weight ratio of said **sugar** or **sugar alcohol** is 2.5 to 50 pts.wt. to one part by weight of the drug, and the micronised drug has an average diameter of less than 1 micron.
Dwg.0/0

L102 ANSWER 57 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1991-016053 [03] WPIX
DNC C1991-006856
TI Water-solubilised metallocene compsns. - contg. **poly ol**, useful for cancer therapy.
DC B05
IN LUCKS, S; MOHR, W; MUELLER, B; MUELLER, E; MUELLER, R; MULLER, B; MULLER, R; MUELLER, B W
PA (MEDA-N) MEDAC GES FUR KLIN; (MEDA-N) MEDAC GES KLINISCHE SPEZIALPRAEPARATE; (MEDA-N) MEDAC GES KLINISCHE; (THRO-N) THROMB-X NV; (MEDA-N) MEDAC GES KLINISCHE SPZEIALPRAPARATE MBH
CYC 26
PI EP 407804 A 19910116 (199103)*
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
DE 3923270 A 19910117 (199104)
AU 9057879 A 19910117 (199110)
FI 9003573 A 19910115 (199117)
HU 55224 T 19910528 (199127)
JP 03128319 A 19910531 (199128)
DE 3923270 C 19910725 (199130)
CA 2021268 A 19920117 (199215)
DD 296417 A 19911205 (199219)
CS 9003490 A2 19920115 (199233) A61K031-28
HU 208073 B 19930830 (199340) A61K031-28
EP 407804 B1 19931103 (199344) DE 7p A61K031-28

R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE

DE 59003304	G	19931209	(199350)		A61K031-28
US 5296237	A	19940322	(199411)	4p	A61K031-28
ES 2059899	T3	19941116	(199501)		A61K031-28
CZ 279046	B6	19941215	(199507)		A61K031-28
IL 94867	A	19950124	(199510)		A61K031-28
FI 95870	B	19951229	(199605)		A61K031-28
SK 278731	B6	19980204	(199818)		A61K031-28
KR 165676	B1	19990115	(200038)		A61K031-28

ADT EP 407804 A EP 1990-112105 19900626; DE 3923270 A DE 1989-3923270 19890714; JP 03128319 A JP 1990-186977 19900713; CS 9003490 A2 CS 1990-3490 19900713; HU 208073 B HU 1990-4199 19900713; EP 407804 B1 EP 1990-112105 19900626; DE 59003304 G DE 1990-503304 19900626, EP 1990-112105 19900626; US 5296237 A Cont of US 1990-552749 19900716, US 1991-810449 19911219; ES 2059899 T3 EP 1990-112105 19900626; CZ 279046 B6 CS 1990-3490 19900713; IL 94867 A IL 1990-94867 19900626; FI 95870 B FI 1990-3573 19900713; SK 278731 B6 CS 1990-3490 19900713; KR 165676 B1 KR 1990-9662 19900628

FDT HU 208073 B Previous Publ. HU 55224; DE 59003304 G Based on EP 407804; ES 2059899 T3 Based on EP 407804; CZ 279046 B6 Previous Publ. CS 9003490; FI 95870 B Previous Publ. FI 9003573; SK 278731 B6 Previous Publ. CS 9003490

PRAI DE 1989-3923270 19890714

REP 1.Jnl.Ref; DE 2923334; DE 3518447; EP 186505; EP 202673; EP 216362; WO 8300868

IC ICM A61K031-28
ICS **A61K009-14**; A61K033-00; A61K041-00; A61K045-02; A61K045-05; A61K047-10; A61K047-26; C07F017-00

AB EP 407804 A UPAB: 19930928
Water-soluble pharmaceutical compsns. are prepd. by mixing a metallocene complex (I with a **polyol** (II), water and opt. additives, and removing the water from the mixt.

Pref. (I) is a Ti, Ta, Hf, Zr, Mo or V complex, esp. titanocene dichloride (Ia). (II) is a glycol, **sugar alcohol** or **carbohydrate**, NaCl is used as an additive. The mixt. comprises 0.02-0.4% (I), 0.5-6% (II), 91.6-99.48% H2O and 0-3% additives, and may be solubilised by sonication, heating and/or addn. of a cosolvent, esp. DMSO or THF. The water is removed by freeze drying.

USE/ADVANTAGE - The compsns. are useful as cytostatic agents for cancer therapy. The compsns. can be diluted with water to give stable clear solns. suitable for **injection**, despite the normally low solubility and stability of (I) in aq. media.

0/0

FS CPI

FA AB; DCN

MC CPI: B05-A01B; B10-A07; B10-E04C; B10-J02; B12-G07

ABEQ DE 3923270 C UPAB: 19930928
Pharmaceutical compsn. comprises one or more metallocene complexes (0.01-2.0 wt.%) as the active cpd(s).; at least one **polyol** (0.1-20.0 wt.%); and opt. additives, e.g. NaCl as an isotonic agent (up to 20 wt.%). Components are dispersed in an aq. medium; and then freeze-dried.

Pref. metallocenes are produced from V, Hf, Zr, Mo, Ta and esp. Ti salts. Typical **polyols** are glycols, **sugar alcohols**, **carbohydrates** and their mixts.

USE - Prods. are cytostatic agents for the treatment of cancer and tumours, having improved stability and solubility in aq. media.

ABEQ EP 407804 B UPAB: 19931213
Pharmaceutical compsn. contg. metallocene complex with increased solubility and rate of dissolution and improved stability, characterised in that it is obtainable by mixing a metallocene complex, a **polyol** , water and optionally additives and subsequently removing the water from the mixt.

Dwg.0/0

ABEQ US 5296237 A UPAB: 19940428
A new water-soluble lyophilised powdered compsn. comprises a metallocene complex of formula (Cp)2MXn-3 (where Cp is cyclopentadienyl anion; M is

transition metal of valency n; and X is mono- or poly-valent anion) and a **polyol**, viz. glycerol, 1,2-propylene glycol, 1,5-pentanediol, polyethylene glycol, a block copolymer of propylene glycol and ethylene glycol, pentaerythritol, **sorbitol, mannitol, glucose, fructose, sucrose, lactose** or mixts., which form soln. in water.

Amt. metallocene complex is 0.01-2 % wt.; water is 58-99.89 % wt.; **polyol** 0.1-20 % wt.; and up to 20 % wt. of isotonicity regulator (e.g. NaCl) in powder. Complexes include metallocenes of Ti, Ta, Hf, Zr, Mo, V, and mixts. pref. TiCl2.

USE - Stabilised soln. contg. 0.05-0.5 mg/ml of metallocene complex for **parenteral** admin. as cytostatic for treatment of tumours.

Dwg.0/0

L102 ANSWER 58 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1990-306636 [41] WPIX
DNN N1990-235756 DNC C1990-132376
TI Multilayered system for **transdermal** drug delivery - has islands of active ingredient in solid soln., dispersed throughout moisture activatable **matrix**.
DC A96 B07 D22 P31 P34 P73
IN HERRMANN, F; HORSTMANN, M
PA (LOHM) LTS LOHMANN THERAPIE-SYSTEME; (LOHM) LTS LOHMANN THERAPIE-SYSTEME GMBH & CO
CYC 30
PI EP 391172 A 19901010 (199041)*
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
DE 3910543 A 19901011 (199042)
AU 9051314 A 19901004 (199047)
NO 9001458 A 19901002 (199049)
CA 2013050 A 19901001 (199051)
PT 93621 A 19910108 (199104)
FI 9001556 A 19901002 (199105)
HU 54062 T 19910128 (199109)
ZA 9002465 A 19910130 (199109)
JP 03027311 A 19910205 (199111)
CS 9001483 A 19911015 (199149)
DD 293266 A 19910829 (199205)
DE 3910543 C2 19930107 (199301) 7p A61L015-44
EP 391172 B1 19930505 (199318) DE 16p A61M035-00
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
DE 59001338 G 19930609 (199324) A61M035-00
US 5230898 A 19930727 (199331) A61K009-70
ES 2055201 T3 19940816 (199434) A61M035-00
IE 65520 B 19951101 (199604) A61M035-00
IL 93956 A 19951231 (199614) A61L015-16
JP 2552191 B2 19961106 (199649) 6p A61K009-70
NO 180671 B 19970217 (199714) A61M037-00
US 5702721 A 19971230 (199807) 8p A61K009-70
CA 2013050 C 19980428 (199828) A61K009-70
CZ 284287 B6 19981014 (199847) A61L015-16
KR 9607517 B1 19960605 (199919) A61M035-00
FI 103478 B1 19990715 (199934) A61L015-44
SK 280782 B6 20000711 (200050) A61M035-00
ADT EP 391172 A EP 1990-105527 19900323; DE 3910543 A DE 1989-3910543 19890401; ZA 9002465 A ZA 1990-2465 19900330; JP 03027311 A JP 1990-77134 19900328; DE 3910543 C2 DE 1989-3910543 19890401; EP 391172 B1 EP 1990-105527 19900323; DE 59001338 G DE 1990-501338 19900323, EP 1990-105527 19900323; US 5230898 A US 1990-500646 19900328; ES 2055201 T3 EP 1990-105527 19900323; IE 65520 B IE 1990-1175 19900330; IL 93956 A IL 1990-93956 19900330; JP 2552191 B2 JP 1990-77134 19900328; NO 180671 B NO 1990-1458 19900330; US 5702721 A Div ex US 1990-500646 19900328, Cont of US 1993-43918 19930407, US 1994-298236 19940830; CA 2013050 C CA 1990-2013050 19900326; CZ 284287 B6 CS 1990-1483 19900327; KR 9607517 B1 KR 1990-4377 19900331; FI 103478 B1 FI 1990-1556 19900328; SK 280782 B6 CS 1990-1483 19900327

FDT DE 59001338 G Based on EP 391172; ES 2055201 T3 Based on EP 391172; JP 2552191 B2 Previous Publ. JP 03027311; NO 180671 B Previous Publ. NO 9001458; US 5702721 A Div ex US 5230898; CZ 284287 B6 Previous Publ. CS 9001483; FI 103478 B1 Previous Publ. FI 9001556; SK 280782 B6 Previous Publ. CS 9001483

PRAI DE 1989-3910543 19890401

REP 1.Jnl.Ref; EP 196769; EP 40861; GB 1361289; US 3996934

IC ICM A61K009-70; A61L015-16; A61L015-44; A61M035-00; A61M037-00
ICS A61B037-00; **A61K009-14**; A61K031-44; A61K045-06; A61K047-30; A61K047-32; A61K047-36; A61L015-42; B32B007-02

AB EP 391172 A UPAB: 19930928
Laminated transdermal therapeutic system comprises a backing layer impermeable to active ingredient (I); a (I)-contg. activatable matrix and a layer which controls entry of skin moisture. The new feature is that the matrix, which can be activated by skin moisture, is made of water-vapour permeable, water-insoluble (I)-free base material in which are distributed 'islands' consisting of a solid soln. of (I) in a water-soluble or swellable base The 'islands' are 0.5-70 (pref. 5-40)% on the wt. of the matrix and one of particle size below 5 microns. They may be aligned in a plane parallel to the release surface. The base material for the island is polyvinyl alcohol, polyvinylpyrrolidone, polymethacrylate acid copolymers, **polysaccharides** and/or polyethylene glycol.
USE/ADVANTAGE - These systems are storage stable and provide a high (I) flux through the skin. Suitable (I) are antihistamines, antirheumatics, opioids, anticholinergics, antisympathomimetics, steroid hormones, prostaglandins, neuroleptics and amphetamines.
1/2

FS CPI GMPI

FA AB; DCN

MC CPI: A12-V01; A12-V03A; B04-B02D1; B04-B02E; B04-C02; B04-C03; B05-B01B; B05-C08; B10-B04B; B12-C05; B12-D01; B12-D06; B12-D09; B12-E02; B12-E04; B12-E05; B12-M02F; D09-C04B

ABEQ DE 3910543 C UPAB: 19930928
Transdermal pharmaceutical compsn. comprises an impermeable support on which is mounted a layer of active component(s) dispersed in a carrier matrix, covered with a skin adhesive moisture permeable film that allows the passage of skin moisture and an outer, detachable protective layer. The active layer comprises a solid soln. of one or more therapeutic agents in a water-soluble or water-swellable carrier, dispersed in a carrier matrix.
USE/ADVANTAGE - The protective film is removed and the adhesive surface is applied to the skin. Moisture from the skin permeates into the active layer to release the active component(s), which diffuse back transdermally, facilitating a controlled dosage of therapeutics.
1/2

ABEQ EP 391172 B UPAB: 19931112
A transdermal therapeutic system exhibiting a layered structure, comprising a backing layer (11), which is substantially impermeable to active substances, and a matrix (12) containing the active substance and being activatable by cutaneous moisture, characterised in that it is provided with a layer (13) controlling the access of cutaneous moisture, and in that the matrix comprises a basis mateiral (15) which is permeable to water vapour, but substantially water-insoluble and mainly free of active substances, in which islands (14) are distributed which consists of a solid solution of drug in a water-soluble or water-swellable basis material.
1/2
Dwg.1/2

ABEQ US 5702721 A UPAB: 19980216
Laminated transdermal therapeutic system comprises a backing layer impermeable to active ingredient (I); a (I)-contg. activatable matrix and a layer which controls entry of skin moisture. The new feature is that the matrix, which can be activated by skin moisture, is made of water-vapour permeable, water-insoluble (I)-free base material in which are distributed 'islands' consisting of a solid soln. of (I) in a

water-soluble or swellable base The 'islands' are 0.5-70 (pref. 5-40)% on the wt. of the matrix and one of particle size below 5 microns. They may be aligned in a plane parallel to the release surface. The base material for the island is polyvinyl alcohol, polyvinylpyrrolidone, polymethacrylate acid copolymers, **polysaccharides** and/or polyethylene glycol.

USE/ADVANTAGE - These systems are storage stable and provide a high (I) flux through the skin. Suitable (I) are antihistamines, antirheumatics, opioids, anticholinergics, antisympathomimetics, steroid hormones, prostaglandins, neuroleptics and amphetamines.

Dwg.0/0

L102 ANSWER 59 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1990-224365 [29] WPIX
DNC C1990-096769
TI Thermally dried emulsion compsns.. - reconstitutable to emulsion, contg. lipid-soluble material, emulsifier and **carbohydrate.**
DC B07 D13
IN SICILIANO, A A; TABIBI, E; SICILLIANO, A
PA (MEDI-N) MEDICONTROL CORP
CYC 14
PI WO 9006746 A 19900628 (199029)*
RW: AT BE CH DE ES FR GB IT LU NL SE
W: JP
CA 2005810 A 19900620 (199036)
EP 449960 A 19911009 (199141)
R: AT BE CH DE ES FR GB IT LI LU NL SE
JP 04504108 W 19920723 (199236) 9p A61K009-14 <--
EP 449960 B1 19930908 (199336) EN 11p A61K009-107
R: AT BE CH DE ES FR GB IT LI LU NL SE
DE 68909057 E 19931014 (199342) A61K009-107
JP 07121858 B2 19951225 (199605) 6p A61K009-14 <--
ADT JP 04504108 W WO 1989-US5632 19891215, JP 1990-501586 19891215; EP 449960 B1 WO 1989-US5632 19891215, EP 1990-901403 19891215; DE 68909057 E DE 1989-609057 19891215, WO 1989-US5632 19891215, EP 1990-901403 19891215; JP 07121858 B2 WO 1989-US5632 19891215, JP 1990-501586 19891215
FDT JP 04504108 W Based on WO 9006746; EP 449960 B1 Based on WO 9006746; DE 68909057 E Based on EP 449960, Based on WO 9006746; JP 07121858 B2 Based on JP 04504108, Based on WO 9006746
PRAI US 1988-287127 19881220; US 1989-409822 19890920
REP CH 414950; EP 211257; EP 276735; FR 2494992; US 3514298
IC ICM A61K009-107; **A61K009-14**
ICS A23D007-00; A23K001-16; A61K009-10; A61K047-36; A61K047-44; B01J013-00
AB WO 9006746 A UPAB: 19930928
Dry compsns. which can be mixed with water to form an o/w emulsion in which the oil phase has an av. droplet dia. below 0.4 microns are produced by drying an o/w emulsion at a temp. of at least 20 deg.C.

The starting emulsion has an av. oil-phase droplet dia. below 0.4 microns and comprises 0.1-60wt.% of a lipid-soluble material (I), 0.1-10wt.% of an o/w emulsifier (II), 0.5-70wt.% of a hydrophilic water-soluble **carbohydrate** (III) and 20-99wt.% water.

USE/ADVANTAGE - The compsns. are intended for oral or **parenteral** use as therapeutics, nutrients or biologics (sic). The compsns. have good storage stability, are easily sterilised, can be reconstituted to various concns., are easily transported and preserved, and yield reconstituted emulsions with a similar droplet size to the original emulsion. Time-consuming freeze drying is avoided.

0/0
FS CPI
FA AB; DCN
MC CPI: B01-D02; B03-L; B04-B01B; B04-B01C; B04-B02C; B04-B02D; B04-B04A4; B04-C02; B04-C03C; **B04-D01**; B05-B01D; B07-A02; B10-B02B; B10-E04A; B10-E04C; B10-G02; D03-H01T
ABEQ EP 449960 B UPAB: 19931122
A solid dehydrated oil-in-water emulsion which is prepared from an initial

completely liquid oil-in-water emulsion which contains a continuous completely liquid aqueous phase, dispersed discontinuous completely liquid oil phase droplets therein, and containing no insoluble solid particulate matter, said droplets having an average diameter of less than about 0.4 microns, wherein (a) the initial oil-in-water emulsion is prepared in the absence of any organic solvent and from a combination consisting of: (i) 0.1 to 60 weight percent of a lipid-soluble material, (ii) 0.1 to 10 weight percent of an oil-in-water emulsifier, (iii) 0.5 to 70 weight percent of a hydrophilic, water-soluble **carbohydrate** which is solid at room temperture, and (iv) 20 to 99 weight percent water, (b) the dehydration is performed at a temperature of at least 20 deg.C; and (c) after addition of water to reconstitute the initial emulsion, a completely liquid oil-in-water emulsion containing no insoluble solid particulate matter and again having dispersed oil phase droplets therein having an average diameter of less than about 0.4 micron is produced.
Dwg.0/0

L102 ANSWER 60 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1989-370553 [50] WPIX
DNC C1989-164083
TI Lyophilised monoclonal antibody compsns. - comprising buffer, antibody and **maltose**.
DC B04
IN MATTIS, J A; PHILLIPS, C P
PA (CENZ) CENTOCOR INC
CYC 12
PI WO 8911297 A 19891130 (198950)* EN 34p
RW: AT BE CH DE FR GB IT LU NL SE
W: JP
EP 417193 A 19910320 (199112)
R: AT BE CH DE FR GB IT LI LU NL SE
JP 03504605 W 19911009 (199147)
EP 417193 B1 19930804 (199331) EN 18p A61K039-395
R: AT BE CH DE FR GB IT LI LU NL SE
DE 68908175 E 19930909 (199337) A61K039-395
ADT WO 8911297 A WO 1989-US2252 19890524; EP 417193 A EP 1989-906925 19890524; JP 03504605 W JP 1989-506569 19890524; EP 417193 B1 EP 1989-906925 19890524, WO 1989-US2252 19890524; DE 68908175 E DE 1989-608175 19890524, EP 1989-906925 19890524, WO 1989-US2252 19890524
FDT EP 417193 B1 Based on WO 8911297; DE 68908175 E Based on EP 417193, Based on WO 8911297
PRAI US 1988-199931 19880527
REP EP 73371; US 4186192; US 4499073; CH 645537; EP 124018
IC **A61K009-14**; A61K039-39; A61K043-00; A61K047-00
ICM A61K039-395
ICS **A61K009-14**; A61K039-39; A61K043-00; A61K047-00
AB WO 8911297 A UPAB: 19930923
Lyophilised monoclonal antibody compsns. comprise a buffer, the antibody (or antibody fragment) and **maltose**. Prodn. of monoclonal antibody formulations is effected by lyophilising the formulation (sic) to form a lyophilisd cake capable of being reconstituted into an **injectable** soln.
USE/ADVANTAGE - Lyophilised radiolabelled antibody compsns. can be reconstituted into **injectable** solns. for scintigraphic imaging of tumours or disease sites. The compsns. can be stored for long periods, even at high temps., without loss of biological activity, and are readily reconstituted to form ppte.-free solns.
0/4
FS CPI
FA AB; DCN
MC CPI: B04-B04C5; B04-B04C6; B07-A02; B11-C07A3; B12-K04A; B12-K04B
ABEQ EP 417193 B UPAB: 19931118
A monoclonal antibody composition for **parenteral** administration of immunoglobulin G comprising a lyophilized formulation of; (a) sodium acetate having a pH of between 3 and 6; (b) **maltose**; and (c) monoclonal immunoglobulin G or a fragment thereof.

Dwg.0/4

L102 ANSWER 61 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1989-324073 [44] WPIX
DNC C1989-143518
TI Tumour necrosis factor formulations - contg. a stabiliser material to maintain biological activity over a range of temps..
DC A96 B04
IN HORA, M S; SMITH, F W; HORA, M; SINGH, M; SMITH, F
PA (SING-I) SINGH M; (CETU) CETUS CORP
CYC 19
PI WO 8909610 A 19891019 (198944)* EN 33p
RW: AT BE CH DE FR GB IT LU NL SE
W: AU DK FI JP KR NO
AU 8934473 A 19891103 (199003)
ES 2013667 A 19900516 (199025)
EP 423244 A 19910424 (199117)
R: AT BE CH DE FR GB IT LI LU NL SE
JP 03504721 W 19911017 (199148)
US 5215743 A 19930601 (199323) 13p A61K045-05
EP 423244 B1 19940302 (199409) EN 22p A61K037-02
R: AT BE CH DE FR GB IT LI LU NL SE
DE 68913537 E 19940407 (199415) A61K037-02
ADT WO 8909610 A WO 1989-US1226 19890322; ES 2013667 A ES 1989-1300 19890413; EP 423244 A EP 1989-909946 19890322; JP 03504721 W JP 1989-504712 19890322; US 5215743 A US 1988-181077 19880413; EP 423244 B1 EP 1989-909946 19890322, WO 1989-US1226 19890322; DE 68913537 E DE 1989-613537 19890322, EP 1989-909946 19890322, WO 1989-US1226 19890322
FDT EP 423244 B1 Based on WO 8909610; DE 68913537 E Based on EP 423244, Based on WO 8909610
PRAI US 1988-181077 19880413
REP FR 2532178; FR 2565490; JP 63126896; 01Jnl.Ref
IC **A61K009-14**; A61K037-02; A61K047-00
ICM A61K037-02; A61K045-05
ICS **A61K009-14**; A61K037-24; A61K047-00
AB WO 8909610 A UPAB: 19930923
A low moisture lyophilised pharmaceutical prepn. with reduced oligomers for reconstituting in an aqs. vehicle for **parenteral** administration to a patient to provide tumour necrosis factor (TNF) therapy is claimed comprising a mixt. of (a) TNF, (b) a wt. excess over the TNF of a stabiliser material (I) that does not effect the stability of the TNF adversely, where (I) is a protein, **polysaccharide**, organic hydrophilic polymer or **oligosaccharide**, (c) a buffer, and (d) a crystallising solute (II), provided that if (I) is an **oligosaccharide**, (II) is present in a wt. ratio with the solute of at least 2.1.

(I) may be e.g. human serum albumin, **dextran**, polyethylene glycol, polysorbate 80, PVP, **sucrose**, **lactose** or **trehalose** and the buffer may be e.g. citrate, phosphate or citrate-phosphate. (II) may be e.g. **mannitol** and the ratio of (I) to (II) is e.g. 2:1 to 3:1. The prepn. may also contain EDTA. Also claimed is a liquid pharmaceutical prepn. having less than 2% TNF oligomer suitable for **parenteral** administration to a patient to provide TNF therapy comprising (a) TNF, (b) a wt. excess over the TNF of a stabiliser material selected from a protein, **polysaccharide**, organic hydrophilic polymer or **oligosaccharide** and (c) a crystallisable buffer.

ADVANTAGE - The TNF formulations maintain the activity of TNF for extended periods of time over a wide range of temps. They retard or greatly reduce TNF oligomer formation thereby imparting low immunogenicity and maintenance of biological activity.

0/5
FS CPI
FA AB; DCN
MC CPI: A12-V01; B04-B04A; B04-B04D2; B04-B04J; B04-C02; B04-C03; **B04-D01**; B07-A02; B10-A07; B12-G07

ABEQ US 5215743 A UPAB: 19931115
Prepn. for **parenteral** admin. to provide TNF therapy comprises: (1) TNF; (2) excess of a stabiliser selected from HSA, **dextran**, PEG, polysorbate 80, PVP, **sucrose**, **lactose** or **trehalose**; (3) buffer e.g. citrate, phosphate or citrate-phosphate; and (4) crystallising solute, provided that if the stabiliser is an **oligosaccharide**, then the solute is at a wt. ratio of 2:1 to 3:1 and is **mannitol** or glycine.
The prepn. pref. comprises 0.25 mg.ml TNF, 10mM phosphate buffer, 10 mg/ml **mannitol** and 20 mg/ml **dextran**.
ADVANTAGE - TNF oligomer formation is prevented, which gives the prepn. low immunogenicity.
Dwg.0/3

ABEQ EP 423244 B UPAB: 19940418
A low moisture lyophilised preparation for use in **parenteral** administration of tumour necrosis factor (TNF) to a patient and having no more than 2.3% TNF oligomers upon reconstitution, the preparation comprising (1) TNF; (2) a weight excess over the TNF of a physiologically acceptable stabiliser material that does not affect the stability of the TNF adversely selected form human serum albumin, **dextran**, polyethylene glycol, polysorbate 80, polyvinylpyrrolidone, **sucrose**, **lactose** or **trehalose**; (3) a physiologically acceptable buffer; and (4) an amount of a physiologically acceptable crystallising solute effective in forming a crystalline matrix during lyophilisation, provided that if the stabiliser material is an **oligosaccharide** said crystallising solute is present in a weight ratio with the stabiliser material of 2;1 to 3:1.
Dwg.0/3

L102 ANSWER 62 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1989-214337 [30] WPIX
DNC C1989-095285
TI Cytostatic anthracycline antibiotics stabilisation - using **lactose** as stabiliser.
DC B05 B07
IN POHLER, W
PA (FARH) HOECHST AG
CYC 19
PI EP 325113 A 19890726 (198930)* DE 7p
R: AT BE CH DE ES FR GB IT LI LU NL SE
DE 3801178 A 19890727 (198931)
AU 8928526 A 19890720 (198936)
NO 8900198 A 19890814 (198938)
DK 8900193 A 19890719 (198939)
ZA 8900331 A 19890927 (198944)
FI 8900211 A 19890719 (198945)
PT 89465 A 19891004 (198945)
JP 02000707 A 19900105 (199007)
ADT EP 325113 A EP 1989-100118 19890105; DE 3801178 A DE 1988-3801178 19880118; ZA 8900331 A ZA 1989-331 19890116; JP 02000707 A JP 1989-6078 19890117
PRAI DE 1988-3801178 19880118
REP 3.Jnl.Ref; DE 2017373; EP 131942; EP 169700; GB 2165751; GB 2178311; JP 60092212
IC **A61K009-14**; A61K031-71; A61K047-00; C07B063-00
AB EP 325113 A UPAB: 19930923
New stabilised dry prepns. of cytostatically active anthracycline antibiotics contain **lactose** as the stabilising agent and a rhodomycinone **hexasaccharide** or **tetrasaccharide** as the antibiotic.
Pref. antibiotics are redorubicin and cytorhodin (pref. cytorhodin A). The prepn. pref. additionally contain a pH regulating cpd..
Prepn. are produced by dry-mixing the antibiotic with the stabiliser or by prepg. a mixed soln. of the antibiotic and **lactose** and drying the soln. by lyophilisation or spray-drying.
USE - Stable powders which can be dissolved in water or a suitable

solvent (e.g. **glucose** soln. or physiological saline) to give a prepn. suitable for **parenteral** administration.
0/0
FS CPI
FA AB; DCN
MC CPI: B02-C01; B02-R; B07-A02; B12-G07; B12-M06; B12-M11G

L102 ANSWER 63 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1986-216099 [33] WPIX
DNC C1986-093182
TI Platelet coagulation inhibitor - contains reducing di **saccharide** and 7-piperidino- 1,2,3,5-tetra hydro imidazo (2,1-B) quinazoline-2-one.
DC B02
PA (DAUC) DAIICHI SEIYAKU CO
CYC 1
PI JP 61148123 A 19860705 (198633)* 5p
JP 04063859 B 19921013 (199245) 4p A61K031-505
ADT JP 61148123 A JP 1984-269472 19841220; JP 04063859 B JP 1984-269472 19841220
FDT JP 04063859 B Based on JP 61148123
PRAI JP 1984-269472 19841220
IC ICM A61K031-505
ICS A61K009-08; **A61K009-14**; A61K031-50; A61K047-26
AB JP 61148123 A UPAB: 19930922
Compsn. consists of a reducing **disaccharide** and 7-piperidino-1,2,3,5 -tetrahydroimidazo (2,1-b) quinazoline-2-one (I) or its salt.
Salt is eq. HCl, HBr, H2SO4, H3PO4, alkyl sulphonic acid, fumaric acid, maleic acid, or succinic acid. Reducing **disaccharide** is, e.g. **maltose**, **lactose**, **cellobiose** or gentiobiose. Drug is lyophilised to stabilise (I). Pref. more than 1.7 times (I) of the **disaccharide** is used. To prepare the lyophilised drug, the soln. is adjusted to pH 2.0-4.0, with concn. of (I) 1.6-30 mg/ml, and concn. of **disaccharide** pref. 40-200 mg/ml.
USE/ADVANTAGE - Compsn. when lyophilised is a stable drug that can prevent platelet coagulation effect. Daily dose for adult is 1-20 mg (p.o.), and 0.1-10 mg (i.v.). LD50 (mice) (i.v.) is 314.5 mg/kg (male)and 380.0 mg/kg (female). (I) is easily sol. in H2O, by **parenteral** use, it has high platelet coagulation prevention effect, and a little effect against the cardiovascular system.
0/0
FS CPI
FA AB
MC CPI: B06-D17; B07-A02; B12-H02

L102 ANSWER 64 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1985-263120 [42] WPIX
CR 1986-225208 [34]
DNC C1985-114038
TI Microbially produced interleukin-2 compsn. - contg. water soluble carrier and surfactant to ensure water solubility.
DC B04 C03 D16
IN FERNANDES, P; TAFORO, T
PA (CETU) CETUS CORP
CYC 12
PI WO 8504328 A 19851010 (198542)* EN 21p
RW: AT BE CH DE FR GB LI NL SE
JP 61500790 W 19860424 (198623)
ZA 8507053 A 19860317 (198627)
EP 211835 A 19870304 (198709) EN
R: AT BE CH DE FR GB NL SE
W: JP
EP 211835 B 19900103 (199002) EN
R: AT BE CH DE FR GB LI NL SE
DE 3575072 G 19900208 (199007)
CA 1283356 C 19910423 (199121)#

JP 04066454 B 19921023 (199247) 8p A61K037-02
JP 05170660 A 19930709 (199332) 8p A61K037-02
JP 06078239 B2 19941005 (199438) 8p A61K037-02
ADT WO 8504328 A WO 1985-US501 19850325; JP 61500790 W JP 1985-501519 19850325; ZA 8507053 A ZA 1985-7053 19850913; EP 211835 A EP 1985-901824 19850325; JP 04066454 B JP 1985-501519 19850325, WO 1985-US501 19850325; JP 05170660 A Div ex JP 1985-501519 19850325, JP 1991-288739 19850325; JP 06078239 B2 Div ex JP 1985-501519 19850325, JP 1991-288739 19850325
FDT JP 04066454 B Based on JP 61500790, Based on WO 8504328; JP 06078239 B2 Based on JP 05170660
PRAI US 1984-594350 19840328
REP 1.Jnl.Ref; EP 109748; EP 91539
IC ICM A61K037-02
ICS A61K009-08; **A61K009-14**
ICA C12P021-00
ICI C12P021-00; C12P021-00, C12R001:
AB WO 8504328 A UPAB: 19941122
Recombinant interleukin-2 (IL-2) compsn. for reconstituting in an aqs. vehicle for **parenteral** administration comprises a sterile lyophilised mixt. of (a) a selectively oxidised and activated microbially produced recombinant IL-2 that is free of non-IL-2 protein, (b) a pharmaceutically acceptable water soluble carrier that does not affect the stability of the IL-2 and (c) a surface active agent to ensure the water solubility of the IL-2/

The surface active agent is pref. sodium dodecyl sulphate (S.S) or sodium deoxycholate. The recombinant IL-2 is pref. des-ala IL-2 ser125 and is present in an amt. of 0.02-3.85 wt.%. The water soluble carrier is pref. **mannitol**.

USE - The compsn. is used for treatment of immunodeficiency states, enhancement of cell-mediated immune responses, treatment of rheumatoid or other inflammatory arthritis, treatment of diseases of abnormal immune respinse such as multiple sclerosis, systemic lupus erthematosis, glomerulonephitis or hepatitis; regulation of haemotopoietic tumours or pre-malignant or aplastic abnormalities of haemotopoietic tissue, as an adjuvant as a mediator of neurotransmission or as a psychoactive therepeutic, as an enkephalin for therepeutic purposes or as a modifier of CNS function.

Dwg.0/1
Dwg.0/1
FS CPI
FA AB
MC CPI: B01-D02; B04-C01; B05-A01B; B10-A07; B10-A09A; B12-A01; B12-A06; B12-C05; B12-C06; B12-C10; B12-D02; B12-D03; B12-D07; B12-E02; B12-G02; B12-G03; B12-G07; D05-H
ABEQ EP 211835 B UPAB: 19930925
A recombinant IL-2 composition suitable for reconstituting in a pharmaceutically acceptable aqueous vehicle for **parenteral** administration to a patient to provide IL-2 therapy characterized by a sterile lyophilized mixture of: (a) a therapeutically effective amount of selectively oxidized microbially produced recombinant IL-2 that is substantially free of non-IL-2 protein; (b) a pharmaceutically acceptable water soluble carrier that does not affect the stability of the oxidized microbially produced IL-2 adversely; and (c) a sufficient amount of a surface active agent to ensure the water solubility of the oxidized, microbially produced recombinant IL-2.
ABEQ JP 92066454 B UPAB: 19930925
Recombinant interleukin-2 (IL-2) compsn. for reconstituting in an aq. vehicle for **parenteral** administration comprises a sterile lyophilised mixt. of (a) a selectively oxidised and activated microbially produced recombinant IL-2 that is free of non-IL-2- protein, (b) a pharmaceutically acceptable water soluble carrier that does not affect the stability of the IL-2 and (c) a surfactant to ensure the water-solubility of the IL-2. The surfactant is pref. sodium dodecyl sulphate (S

L102 ANSWER 65 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1985-111858 [19] WPIX

CR 1985-100425 [17]; 1985-106422 [18]; 1986-311723 [48]; 1988-149707 [22]
DNC C1985-048334
TI Sustained release **injectable** compsn. - consists of bio-degradable powder contg. the active ingredient suspended in viscous liq..
DC B04 B05 B07 C03 P32
IN FUJIOKA, K; SATO, S; YAMAHIRA, Y; YOSHIDA, N; TAKADA, Y
PA (SUMO) SUMITOMO CHEM CO LTD; (SUMU) SUMITOMO PHARM CO LTD; (SUMO) SUMITOMO CHEM IND KK
CYC 9
PI EP 140255 A 19850508 (198519)* EN 17p
R: CH DE FR GB LI SE
JP 60112713 A 19850619 (198531)
EP 140255 B 19910515 (199120)
R: CH DE FR GB LI SE
DE 3484584 G 19910620 (199126)
JP 05012328 B 19930217 (199310) 4p A61K009-08
US 5385738 A 19950131 (199511) 7p A61K009-14 <--
ADT EP 140255 A EP 1984-112313 19841012; JP 60112713 A JP 1983-220452 19831121; JP 05012328 B JP 1983-220452 19831121; US 5385738 A CIP of US 1984-660044 19841012, Cont of US 1986-849968 19860410, Cont of US 1990-488531 19900228, US 1992-844929 19920304
FDT JP 05012328 B Based on JP 60112713
PRAI JP 1983-193064 19831014; JP 1983-197181 19831020; JP 1983-206226 19831101; JP 1983-220452 19831121; JP 1985-77250 19850411
REP A3...8544; BE 882541; FR 2342741; FR 2353285; GB 642385; No-SR.Pub; US 2518510
IC ICM A61K009-08; **A61K009-14**
ICS A61F002-02; A61K009-50; A61K047-00; B01J013-02
ICA A61K045-02
AB EP 140255 A UPAB: 19950508
Compsn. consists of a suspension of a powder consisting of an active ingredient and a biodegradable carrier in a viscous solvent. The carrier may be a collagen, gelatin, albumin, **polysaccharides** such as chitin, polymers such as polyglycolic acid, polylactic acid or polyglutamic acid of which collagen is preferred.
The scope of these is unlimited, but the invention is partic. applicable to those medicaments which cannot be produced in conventional sustained release **injectable** forms or are only slightly soluble in water but are effect in only small amounts. Substances in these categories include prostaglandins, biohormones, bleomycins, mitomycins, tespanin, interferon, interleukin, tumour necrosis factor, indomethacin, adriamycin and 4-carbamoyl-5-hydroxy imidazole.
Dwg.0/0
Dwg.0/0
FS CPI GMPI
FA AB
MC CPI: B04-B04A; B04-C02; B04-C03; B12-M07; B12-M10
ABEQ EP 138216 B UPAB: 19930925
A sustained-release preparation for **parenteral** administration, which comprises interferon as an active ingredient in admixture with a pharmaceutically acceptable biodegradable protein as carrier, said preparation being in the form of powder particles or in the form of a shaped preparation, with the proviso that the form is neither needle-like nor bar-like.
0/1
ABEQ EP 140255 B UPAB: 19930925
A sustained-release **injection** preparation, which comprises a suspension of a powdery mixture in a viscous suspension medium for **injection** preparation, said powdery mixture comprising a pharmaceutically acceptable biodegradable carrier selected from collagen, atelocollagen, a mixture of them, and a mixture thereof with gelatin and a usual amount of a pharamaceutically active ingredient incorporated into said carrier.
ABEQ US 5385738 A UPAB: 19950322
Sustained-release preparation comprises a suspension of a powder in an

injectable viscous solvent. The powder comprises an active agent and a biodegradable carrier selected from proteins, **polysaccharides** and synthetic high molecular cpds. The active agent is pref. indomethacin, bio-hormones, interferons, interleukins, tumour necrosis factor or other cytokines. The carrier is esp. collagen, gelatin, albumin, chitin, polyglycolic acid or polylactic acid.

USE/ADVANTAGE - The active agent is released at an effective level for a long period of time. The compsn. is esp. suitable for medicaments which are unstable to heat and no specific **binding** agent or heating steps are required in the prepn. of the compsn.

Dwg.0/1

L102 ANSWER 66 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1985-100425 [17] WPIX
CR 1985-106422 [18]; 1985-111858 [19]; 1986-311723 [48]; 1988-149707 [22]
DNC C1985-043388
TI Sustained release compsn. of indomethacin, interferon - or 4-carbamoyl-imidazolium-5-ol ate, in biodegradable carrier, e.g. collagen.
DC B04 B05 B07 C03 P32
IN FUJIOKA, K; SATO, S; YAMAHIRA, Y; YOSHIDA, N; YAMASHIRA, Y; TAKADA, Y
PA (SUMU) SUMITOMO PHARM CO LTD; (SUMO) SUMITOMO CHEM CO LTD
CYC 11
PI EP 138216 A 19850424 (198517)* EN 27p
R: CH DE FR GB LI SE
JP 60084213 A 19850513 (198525)
JP 60089418 A 19850520 (198526)
JP 60097918 A 19850531 (198528)
US 4855134 A 19890808 (198939)
JP 03072046 B 19911115 (199150)
US 5081156 A 19920114 (199206)
EP 138216 B1 19930107 (199302) EN 7p A61K009-22
R: CH DE FR GB LI SE
DE 3486029 G 19930218 (199308) A61K009-22
US 5385738 A 19950131 (199511) 7p A61K009-14 <--
ADT EP 138216 A EP 1984-112312 19841012; JP 60084213 A JP 1983-197181 19831020; JP 60089418 A JP 1983-193064 19831014; JP 60097918 A JP 1983-206226 19831101; US 4855134 A US 1986-855387 19860424; JP 03072046 B JP 1983-206226 19831101; US 5081156 A US 1989-358157 19890530; EP 138216 B1 EP 1984-112312 19841012; DE 3486029 G DE 1984-3486029 19841012, EP 1984-112312 19841012; US 5385738 A CIP of US 1984-660044 19841012, Cont of US 1986-849968 19860410, Cont of US 1990-488531 19900228, US 1992-844929 19920304
FDT DE 3486029 G Based on EP 138216
PRAI JP 1983-193064 19831014; JP 1983-197181 19831020; JP 1983-206226 19831101; JP 1983-220452 19831121; JP 1983-236996 19831214; JP 1985-77250 19850411
REP A3...8544; DE 3104815; EP 134289; EP 94157; EP 98110; GB 2042888; GB 2067072; No-SR.Pub; US 4181731; WO 8301198
IC ICM **A61K009-14**; A61K009-22
ICS A61F002-02; A61K009-50; A61K031-40; A61K037-66; A61K045-02; A61K047-00; B01J013-02
AB EP 138216 A UPAB: 19950508
Sustained release compsn. comprises indomethacin (I), interferon (II) or 4-carbamoyl-imidazolium-5-olate (III) as active ingredient, and a biodegradable carrier. The carrier may be a protein, **polysaccharide** or synthetic high mol. cpds. It is pref. collagen, atelocollagen, gelatin, albumin or chitin.

USE/ADVANTAGE - Compsns. may be administered **parenterally** giving maintained levels of the active ingredient in the blood for long periods. The carrier does not accumulate in the body. (I) is a non-steroidal antirheumatic agent with local antiinflammatory activity. (II) is an antiviral and antitumour agent. (III) is an antitumour agent, which inhibits purine synthesis.

Dwg.0/4
Dwg.0/4
FS CPI GMPI

FA AB
MC CPI: B02-V; B06-D01; B07-D09; B12-A06; B12-D07; B12-D09; B12-G07; B12-M10
ABEQ EP 138216 B UPAB: 19930925
A sustained-release preparation for **parenteral** administration, which comprises interferon as an active ingredient in admixture with a pharmaceutically acceptable biodegradable protein as carrier, said preparation being in the form of powder particles or in the form of a shaped preparation, with the proviso that the form is neither needle-like nor bar-like.
0/1
ABEQ US 4855134 A UPAB: 19930925
Sustained-release prepn. comprises interferon, as an active ingredient, and collagen, as a carrier. The prepn. is in the form of powder particles suspended in a viscous solvent suitable for **injection;** or is in the form of a shaped prepn. suitable for use as an **injection** in a solid state or for implanting into a body.
Pref. the interferon is alpha-interferon. Pref. the new prepn. is prepd. by a) mixing interferon and collagen to form a liq. mixt.; and drying the resultant mixt.
ADVANTAGE - New prepn. can maintain the desired level of active ingredient in blood or in a lesional region for a long time.
ABEQ US 5081156 A UPAB: 19930925
Sustained-release compsns. comprise indomethacin or its salt as active ingredient and collagen as carrier, the compsns. being prepd. by: (a) mixing the components to form a liq. mixt. and (b) drying the mixt. without heat treatment. Pref. the compsns. contain 0.5-500 mg of indomethacin or its salt per dosage unit. Pref. they also contain a small amt. of gelatin.
USE/ADVANTAGE - As antiinflammatory agents vs. local inflammation while avoiding undesirable side effects on the CNS and peptic organs.
ABEQ US 5385738 A UPAB: 19950322
Sustained-release preparation comprises a suspension of a powder in an **injectable** viscous solvent. The powder comprises an active agent and a biodegradable carrier selected from proteins, **polysaccharides** and synthetic high molecular cpds. The active agent is pref. indomethacin, bio-hormones, interferons, interleukins, tumour necrosis factor or other cytokines. The carrier is esp. collagen, gelatin, albumin, chitin, polyglycolic acid or polylactic acid.
USE/ADVANTAGE - The active agent is released at an effective level for a long period of time. The compsn. is esp. suitable for medicaments which are unstable to heat and no specific **binding** agent or heating steps are required in the prepn. of the compsn.
Dwg.0/1

L102 ANSWER 67 OF 68 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1979-22071B [12] WPIX
TI Materials inducing cholera antibody formation - comprise support coated with ganglioside and then with cholera toxin.
DC A96 B04
PA (INMR) INST MERIEUX
CYC 12
PI BE 870564 A 19790319 (197912)*
GB 2004186 A 19790328 (197913)
DE 2840506 A 19790329 (197914)
NL 7809485 A 19790321 (197914)
DK 7804113 A 19790417 (197919)
NO 7803153 A 19790417 (197919)
SE 7809788 A 19790423 (197919)
JP 54055718 A 19790504 (197924)
FR 2403081 A 19790518 (197925)
US 4303638 A 19811201 (198151)
GB 2004186 B 19820714 (198228)
CH 633447 A 19821215 (198303)
IT 1174425 B 19870701 (199025)
PRAI FR 1977-28162 19770919
IC **A61K009-14**; A61K031-70; A61K039-02; A61K047-00; C07H015-10

AB BE 870564 A UPAB: 19930901
Immunogenic materials comprise support particles coated with a first layer of a ganglioside or ganglioside deriv. with affinity for cholera toxin, and a second layer of cholera toxin.
The support particles can be exthrocytes, bacterial cells (esp. inactivated Vibrio cholerae cells), synthetic or natural polymer latex particles, carbon particles opt. modified **polysaccharide** particles, or porous mineral particles coated with opt. crosslinked, opt. modified **polysaccharides**.
The first layer pref. comprises ganglioside Gm1, lysoganglioside Gm1, a partial hydrolysis product of ganglioside Gm1, or a mono- or a-sialo ganglioside prepd. by acid hydrolysis of gangliosides or their derivs.
The materials can be used as orally or **parenterally** administrable anti-cholera **vaccines** or for isolating anti-cholera antibodies for use as serological reagents.
FS CPI
FA AB
MC CPI: A12-V01; B02-V; B04-B01B; B04-B02B; B04-B04A; B04-B04C; B04-C02; B04-C03; B05-C06

L102 ANSWER 68 OF 68. WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1976-21021X [12] WPIX
TI 2,2'-Anhydro-1-beta-D-arabinofuranosyl-cytosine salts prepns - obtd by freeze drying aq solns. contg specified additives, for **parenteral** leukaemia treatment.
DC B03
PA (KOJK) KOJIN KK
CYC 2
PI DE 2441761 A 19760311 (197612)*
FR 2285855 A 19760528 (197628)
PRAI DE 1974-2441761 19740830
IC **A61K009-14**; A61K031-70
AB DE 2441761 A UPAB: 19930901
Freeze-dried prepns. contg. 2,2'-anhydro-1-beta-D-arabinofuranosyl-cytosine salts (I) are prepd. by freeze-drying an aq. soln. of (I) contg. (a) 0.1-6 wt.%, based on (I), of a **saccharide**, (b) 0.1-6 wt.% of polyvinylpyrrolidone (PVP), (c) 0.1-6 wt.% of sodium carboxymethylcellulose (NaCMC) and/or (d) 0.01-0.05 wt.% of a nonionic wetting agent. The products can be used to prepare **injectable** solns. for use in leukaemia treatment. The prepns. have good storage stability, can be prepd. by conventional rapid freeze-drying, and have a water-solubility of >=1 g/10 ml, forming clear solns.
FS CPI
FA AB
MC CPI: B04-B03; B04-C02; B04-C03; **B04-D01**; B12-G05; B12-M11

=> d his

(FILE 'HOME' ENTERED AT 15:49:51 ON 19 JUL 2001)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 15:50:02 ON 19 JUL 2001
E DK99-514/AP,PRN
L1 1 S E4
L2 74390 S CARBOHYDRATE#/CW
L3 59487 S (SACCHARIDE# OR MONOSACCHARIDE# OR DISACCHARIDE# OR TRISACCHA
L4 128138 S L2,L3
L5 11017 S SUGAR (L) ALCOHOL
L6 467481 S MALTOSE OR SUCROSE OR LACTOSE OR CELLOBIOSE OR TREHALOSE OR M
L7 64153 S DEXTRAN OR MANNOSE OR SORBOSE OR MELIBIOSE OR SOPHROSE OR TUR
L8 1039 S ALDITOL#/CW

FILE 'REGISTRY' ENTERED AT 15:54:57 ON 19 JUL 2001
L9 18 S (MALTOSE OR SUCROSE OR LACTOSE OR CELLOBIOSE OR TREHALOSE OR
L10 12 S (DEXTRAN OR MANNOSE OR SORBOSE OR MELIBIOSE OR SOPHROSE OR TU

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     FILE 'HCAPLUS' ENTERED AT 15:55:38 ON 19 JUL 2001
L11      194521 S L9,L10
L12      605033 S L4-L8,L11
L13       37232 S PHARMACEUTICAL?/SC,SX,CW AND L12
L14         895 S L13 AND BINDER
L15        1151 S L13 AND PARENTERAL?
L16           5 S L14 AND L15
L17         483 S L13 AND PELLET?
L18          68 S L14 AND L17
L19          71 S L16,L18
L20          66 S L19 AND 63/SC
                E DRUG DELIVERY SYSTEM/CT
                E E4+ALL
L21        5827 S E3 AND L13 AND 63/SC
L22         167 S E39-E41 AND L13 AND 63/SC
L23          36 S E42-E43 AND L13 AND 63/SC
L24          52 S E65 AND L13 AND 63/SC
L25          69 S E66 AND L13 AND 63/SC
L26        5593 S E2+NT AND L13 AND 63/SC
L27         480 S L14 AND L21-L26
L28           3 S L27 AND L15
L29           9 S L27 AND INJECT?
L30          11 S L28,L29

     FILE 'REGISTRY' ENTERED AT 16:03:49 ON 19 JUL 2001
L31           1 S SOPHOROSE/CN

     FILE 'HCAPLUS' ENTERED AT 16:04:00 ON 19 JUL 2001
L32         487 S L31 OR SOPHOROSE
L33           6 S L32 AND E2+NT
L34           0 S L32 AND E3
L35           4 S L33 AND 63/SC
L36           1 S L35 AND PARENTER?
L37           1 S L35 AND PELLET?
L38           1 S L35 AND INJECT?
L39          11 S L30,L36-L38
L40           1 S L1 AND L39
L41        3220 S L12,L32 AND PARENTER?
L42        3426 S L12,L32 AND PELLET?
L43         828 S L41,L42 AND INJECT?
L44          47 S L43 AND BIND?
L45          45 S L44 NOT L39
L46           2 S L45 AND (GENE THERAPY OR SUSTAIN? RELEAS?)/TI
L47           3 S L40,L46
L48           3 S L47 AND (L1-L8,L11-L30,L32-L46 OR POLYOL OR CARBOHYDRATE OR ?
                E BUCH RASMUSSEN T/AU
L49          21 S E3,E4
                E AASMUL S/AU
L50           3 S E4
                E POULSEN J/AU
L51          13 S E3,E29
                E FLINK J/AU
L52          52 S E3-E7
                E HANSEN P/AU
L53         748 S E3-E40
                E HANSEN PHIL/AU
L54          27 S E4-E11
                E JUUL MORTENSEN C/AU
L55           3 S E4
L56          52 S L12,L32 AND L49-L55
L57           1 S L56 AND PARENTER?
L58           1 S L56 AND ?PELLET?
L59           3 S L56 AND BIND?
L60           6 S L56 AND 63/SC
L61           8 S L57-L60
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L62           6 S L61 AND L60
L63           8 S L48,L62
L64          20 S L41,L42 AND AMORPHOUS?
L65           3 S L64 AND INJECT?
L66           0 S L64 AND DEVICE
L67           2 S L64 AND BIND?
L68           4 S L65,L67
L69           1 S L68 AND 63/SC
L70          10 S L64 AND 63/SC
L71           9 S L70 NOT L68
                SEL DN 3 7 8
L72           6 S L71 NOT E1-E3
L73          14 S L63,L69,L72

     FILE 'HCAPLUS' ENTERED AT 16:32:17 ON 19 JUL 2001
L74           4 S ?MALTIDEX?
L75           3 S L74 NOT L73

     FILE 'WPIX' ENTERED AT 16:34:28 ON 19 JUL 2001
L76           1 S ?MALTIDEX?
                E DK99-514/AP,PRN
L77           1 S E4
L78        3002 S A61K009-14/IC,ICM,ICS
L79       47494 S L6,L7 OR SOPHOROSE
L80       38535 S CARBOHYDRATE OR ?SACCHARID? OR SUGAR(L)ALCOHOL
L81       31359 S POLYOL OR POLY OL
L82        5638 S (B04-D01 OR C04-D01)/MC
L83         717 S L78 AND L79-L82
L84          57 S L83 AND N104/M0,M1,M2,M3,M4,M5,M6
L85         591 S L83 AND M782/M0,M1,M2,M3,M4,M5,M6
L86          47 S L83 AND (P843 OR M424 OR M740)/M0,M1,M2,M3,M4,M5,M6
L87          58 S L83 AND N103/M0,M1,M2,M3,M4,M5,M6
L88          53 S L85 AND L87
L89          48 S L85 AND L84
L90          40 S L85 AND L86
L91         106 S L88-L90
L92          30 S PARENTER? AND L85
L93          25 S AMORPH? AND L85
L94           5 S L92,L93 AND BIND?
L95          17 S L92,L93 AND (INJECT? OR VACCIN?)
L96           3 S L92,L93 AND ?PELLET?
L97           3 S L95,L96 AND L94
L98          52 S L92,L93,L95
L99          52 S L77,L97,L98
L100         95 S L91 NOT L99
L101         16 S L100 AND (MATRIX OR PENETRAT? OR MICRONI? OR TRANSDERMAL OR P
L102         68 S L99,L101

     FILE 'WPIX' ENTERED AT 16:54:54 ON 19 JUL 2001
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